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In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

DISEASES OF THE BLOOD

The blood in health and various morbid conditions. Morawitz discusses the question whether there is any difference between the processes of coagulation and of cessation of bleeding. The theory is that wound closure takes place by platelet agglutination rather than by the fibrin coagulation which can be studied *in vitro*. This is based on estimations of the bleeding time by Duke's method, which are not always the same as the coagulation time for the same patient.

Morawitz suggests that in doubtful cases the bleeding time should always be estimated before the coagulation time. If it is normal, i. e. two to three minutes, coagulation is likely to be normal also. If it is prolonged the coagulation time should now be estimated. Prolonged bleeding time he finds to be frequently associated with lessened resistance of the vessels, so that the Rumpel-Leede phenomenon can be evoked. In such cases thrombosis is more to be apprehended than any other abnormality. Prolonged coagulation time is associated with other syndromes. Morawitz believes that thrombosis depends on injury to the vessel wall, e. g. by sepsis, and does not occur merely from prolonged rest.

Graff has investigated the distribution of the red and white cells and their relative proportions in different parts of the body. His observations have been made on histologically healthy organs. He finds that the proportion of red and white cells is very variable in different organs and in different parts of the same organ. He also finds that the condition of the peripheral circulation is no safe guide to that of the internal organs. In case of peripheral hypoleucocytosis there was more often than not internal hyperleucocytosis. Graff concludes that leucocytosis should be considered as of a dual nature, i. e. either due to actual formative increase of the bone-marrow, or due merely to a local accumulation of leucocytes determined by the needs of a particular organ, or by some as yet unknown factor. In the same way leucopenia can depend on marrow failure or on a 'displaced leucocytosis' of some remote organ.

Lampe and Saupe have examined the blood of 50 persons, all members of the Dresden Hospital personnel. They compare the findings with those published in 1918, and conclude that there is a lowering of the total leucocyte count from 9,300 to 8,100, but that the differential count is not much changed. There is still a higher lymphocyte percentage than before the war. These differences are attributed to a too largely carbohydrate diet and to nervous worry.

Buckman and Hallisey detail a new method of platelet counting. The blood is obtained from a vein and allowed to flow into a miniature paraffined transfusion tube. From this it is taken up into an ordinary diluting pipette. The diluting fluid is made as follows: 6 gm. of glucose and 0·4 gm. of sodium citrate are dissolved in 100 c.cm. of distilled water. The solution is filtered. To the filtrate is added about 0·02 gm. of neutral red. When the solution (which is slow) is complete, 0·1 gm. of crystal violet is added and the solution is heated to 60° C. and kept five minutes at that temperature. It is then cooled slowly to room temperature and centrifuged ten minutes at 2,000 revolutions. The supernatant fluid is then twice filtered, each time through three thicknesses of dry No. 30 Whatman paper. The solution is preserved by the addition of 0·2 c.cm. of formaldehyde solution and keeps indefinitely. The platelet counts made from dilutions with this fluid are similar to those with other methods, the mean of nine healthy persons being about 270,000. In spite of the title the paper does not discuss the properties of blood-platelets.

In previous communications, Nonnenbruch and Szyszka have reported how great an influence is exercised on coagulation acceleration by intravenous or intramuscular injections of ethylene-diamin in certain acid compounds, and it was judged by certain animal experiments that the spleen must play an important part in this influence. Stephan found, too, that X-rays applied to the spleen for about five hours, accelerated coagulability so that attempts were made to see whether simple application of warmth to the splenic region, or by heat rays, a like influence could be attained. Results proved this to be the case, and blood coagulability was markedly and regularly accelerated.

The technique of treatment is simple—one electrode was placed over the splenic region, the other on the back, and a bearable heat applied. Fonio's method was used to determine the coagulation—blood being taken from the veins with a dry syringe and six drops placed in a time glass. The time of the first appearance of a fibrinous thread is determined by the pulling through of a glass thread (reaction period). Tables are given showing the time of reaction period and complete coagulation after 18 and 10 minutes' heat application. The results proved that in all cases this treatment markedly increased coagulability, and the cause may be attributed to considerable increase of fibrin ferment in the blood, and was proved by Fonio's $MgSO_4$ series, and by Wohlgemuth's and Stephan's methods of determining fibrin ferment.

Criado and Padilla have examined 15 persons in order to verify the observation of Hasselbach and Heyerdahl that the upright position was associated with a smaller number of leucocytes than decubitus. This they were unable to do, but found, on the contrary, an increased leucocytosis in the upright posture. The increase varied in this series from 100 to 3,000. It was present in blood taken directly from a vein as well as in finger blood. Criado and Padilla are inclined to regard it as due to nervous influences.

Audain states that the normal defence of the body against infecting agents is of two sorts. The first is a local lymphocytic reaction and is active when lymphoid tissues are attacked. The second is a polynuclear reaction and comes into play when non-lymphoid tissues, e.g. the peritoneum, are involved. It may also come into action for a short time pending the full development of lymphoid reaction. Audain maintains that repeated examinations of the blood are thus of very definite value as affording evidence of the degree and kind of response. But is there no leucocytosis in suppurating glands?

Gelera concludes with regard to the complement-value (i.e. the complement content) of the blood that:

1. It is an index of organic reaction or resistance.
2. It is parallel to the amount of leucocytosis and of resulting leucocytolysis.
3. It has little diagnostic but considerable prognostic value.
4. One may properly employ substances which stimulate leucocytosis in the therapeutic management of the later stages of infective diseases.

He notes, in conclusion, some further experiments which show that the serum of a rabbit submitted to repeated subcutaneous injections of foreign leucocytes does not exhibit any leucocytolytic properties, shows very weak precipitin development, and does not cause anaphylactic phenomena following injection of white cells.

Kleiner describes a test for the amount of sugar in the blood which requires only 0·2 c.cm. of blood. The blood is oxalated and filtered, the supernatant or filtered fluid being mixed with picrate-picric acid solution and compared with a standard colour glass in a special colorimeter. Great accuracy is claimed.

Leger describes the reduction of platelets in malaria and their increased numbers in ankylostomiasis. His cases are few but are sufficient to demonstrate a reduction of platelets at the time of the malarial paroxysm with a subsequent reactionary rise. The latter may exceed normal numbers but returns to normal in a few days. This reduction of platelets is a general rule in parasitic diseases of the blood, but filariasis appears to be an exception. Leger concludes by quoting the observation of Aynaud to the effect that we are still unaware of the purposes for which platelets exist.

Escomel has studied the conditions in which parasites are found in the blood by a new method. He lakes the blood with 1 per cent. acetic acid and examines the residue suitably stained. He distinguishes three classes of case, namely, (1) cases in which the parasite lives in the blood; (2) cases in which the parasite lives in the tissues but is at times found as a trespasser in the blood; and (3) cases in which persons in excellent health are nevertheless found to have some degree of haemoparasitism. One or two cubic centimetres of blood are examined, and Escomel considers that his method may be of use to surgeons about to explore septic cases, or cases which might subsequently become septic from germs already in circulation. Incidentally his work would appear to confirm the contention of Kidd that slight haemoparasitism is a normal feature of our careers.

Pittaluga has studied the relationships between the glands of internal secretion and various blood conditions. He finds three main groups of diseases in which both internal secretions and the blood-forming organs show changes more or less interdependent. These are: (1) Diseases of the glands of internal secretion, in which certain haematological abnormalities (morphological or biochemical) appear but are scarcely to be classed as characteristic of these particular diseases since they occur in many conditions. Such are the lymphocytosis and left-handed Arneth shift of hyperthyroidism and hyperadrenalism and the eosinophilia of vagotonic syndromes. (2) Blood diseases proper in which one can by appropriate examination discern some associated endocrine disorder. These include especially lymphatism, the anaemias of childhood and infancy, possibly the leukaemias. Pittaluga is unable to state whether or no pernicious anaemia should be placed in this group. (3) A group intermediate between the two former including what

Pittaluga has named 'the haemodystrophias'. In this group an evident participation of one or more endocrine organs is almost always associated with a hereditary factor, as is the case, for example, in chlorosis, the haemorrhagic diathesis, the eosinophil diathesis, &c.

Trott, of Baltimore, has found that subcutaneous injection of 4 to 8 minims of epinephrin will quickly produce a rise in the leucocyte count, and cause an absolute lymphocytosis in hyperthyroid individuals. She concludes from this experiment that in toxic goitre an increase in the lymphocytes is not always present, especially in the border-line cases. A normal differential count is often found, and in some cases a polymorphonuclear leucocytosis exists.

Sprunt and Evans call attention to those rare cases in which infective disorders are accompanied not by the usual polynuclear leucocytosis but by a lymphocytosis, and generally by some degree of the tissue changes and blood findings of a chronic or subacute leukaemia. It is a fact, as they remark, that these cases are well known to haematologists but have but little recognition from others. The first case was that of a woman student aged 23, who was admitted to hospital with febrile and catarrhal symptoms with no very definite primary localization. A week later pharyngitis developed, and a few days previous to this chains of enlarged lymph glands had been noted in the left anterior and posterior cervical regions. But even when first admitted the liver had been found enlarged. The blood changes showed a total white cell count which reached 17,500 at the highest point but was usually within the normal range. She recovered, but a few months later had a further indisposition with tender cervical glands. At this time her polymorphs were 56 per cent., and abnormal cells which could not be classified 10 per cent. Five years later she was normal in every way.

Another case was that of a medical student aged 24, who was supposed to have an attack of influenza. The spleen was palpable and slight fever lasted more than five weeks. The blood showed a normal total count and 56·7 per cent. of lymphocytes. On one occasion there were abnormal cells reaching 8·8 per cent. Four years later he was normal.

The other four cases are examples of the same syndrome, of which the salient features may be said to include: (1) an onset which is subacute in most cases; (2) an indefinite febrile disorder; (3) commonly chronic tonsillar or pharyngeal infection; (4) slight enlargement of spleen, liver, and glands, or of some of them; (5) a blood picture showing an increase of the total count in the early stages, and later a normal number; (6) a differential count showing an increase of mononuclear elements, some of which are impossible to classify. The authors claim that this blood picture is generally allowed to be of lymphoid origin, a claim which can be admitted with the proviso that the general opinion is probably erroneous. They finally conclude as follows: (*a*) In addition to the mononuclear leucocytosis seen commonly in children, one may encounter occasionally a mononuclear leucocytosis in adults in reaction to acute infection; (*b*) this is not a simple lymphocytosis as in children, but is made up largely of pathological forms, probably all lymphoid in origin; (*c*) among the cases in adults there occurs a group with symptoms and signs so much alike that they may be considered provisionally as a clinical entity; (*d*) when first seen during the febrile period, especially in the early stages, these cases cannot be differentiated with assurance from leukaemia, but the subsequent course makes the diagnosis clear; (*e*) the prognosis, so far as may be judged from a series of six cases, is good.

Pernicious anaemia. Eason made an inquiry regarding the age and sex incidence of pernicious anaemia, with the following results: (1) Edinburgh hospitals showed the largest numbers between the ages of 45 and 59. (2) The rate in these hospitals per 100,000 of the population was highest between 55 and 69. (3) The pernicious anaemia death-rate figures for Scotland corresponded very closely with the Edinburgh hospital case figures. (4) Until the age of 50 the rate of incidence inclined to be higher in the female than in the male. Thereafter the rate was definitely higher in males than in females. (5) Senility is a more important factor than has hitherto been generally recognized. (6) There appears to be an increasing liability to pernicious anaemia with advancing years.

Curschmann, of the Rostock Medical Clinic, also maintains that pernicious anaemia is by no means so rare in old age as is generally supposed. Examination of the records of the Rostock Medical Clinic from 1914 to 1920 showed that there were no less than 13 cases between 61 and 78. The occurrence of pernicious anaemia at this age is not due to the war, as Curschmann had seen some cases before 1914 in Mayence and Rhenish Hesse. Not unfrequently the condition is disguised under the form of senile cachexia and cardiac insufficiency. Curschmann recommends that every case of senile glossodynia should have the blood examined for pernicious anaemia. The condition is amenable to energetic arsenic treatment, as in middle age, and long remissions can be obtained thereby.

Ballmann, of the Fulda Municipal Hospital, reports four cases of pernicious anaemia resembling that recently published by Curschmann (vide *Medical Science*, 1921, **3**, 395) in which symptoms of spinal disease were not a late complication but occurred at a very early stage of the disease, and so dominated the clinical picture that a disease of the blood was not at first suspected. It could not be determined whether the occurrence of so many cases within a few months was a mere coincidence or whether this form of pernicious anaemia with early spinal symptoms had not become more frequent owing to a general diminution of resistance in the central nervous system caused by the mental and physical strain due to the war. Ballmann recommends that on the occurrence of spinal symptoms, the significance of which is not absolutely clear, a careful examination of the blood should be made, as thereby pernicious anaemia may be found to be the underlying disease.

Brandes records four cases of undoubted pernicious anaemia in which cancer of the stomach was found *post mortem*. It could not be definitely settled whether pernicious anaemia or carcinoma was the primary disease. In two of the cases pernicious anaemia was perhaps responsible for the development of carcinoma, and in the other two cases the carcinoma appeared to favour the development of pernicious anaemia.

Miller reports the case of a man aged 31 who was diagnosed as a case of pernicious anaemia 18 months before his death. He had a complete remission following treatment, and his blood became normal. He died not long after operation, which had revealed an inoperable cancer of the stomach. This took the form of a pedunculated papilloma without malignant involvement of the wall of the stomach but with large glandular and hepatic metastases. Miller is inclined to think it possible that the early anaemia was due to an overlooked intragastric haemorrhage. Such haemorrhages certainly occur in cases of papilloma of the stomach, and the acute and almost fatal nature of the anaemia suggests that this was the case.

Carr has studied the records of 148 cases diagnosed as pernicious anaemia at the Cook County Hospital. Of the 22 cases which went to autopsy five proved not to be pernicious anaemia. Four out of 46 cases gave a positive Wassermann reaction. In ten cases the liver was palpable as much as three fingers' breadth below the costal arch. Such considerations tend to invalidate the conclusions drawn. Carr points out that 'the blood picture of pernicious anaemia may be presented exactly as the result of some definite septic, toxic, or malignant condition', and finally makes the diagnosis depend on the failure to discover a cause as much as on the clinical or haematological findings. Of his 148 cases as many as 26 showed sufficiently marked involvement of the nervous system to be classed apart on this account, and only one of these was less than 40 years of age.

O. Weber records several cases of pernicious anaemia and other forms of severe anaemia treated by intravenous or intramuscular injection of colloid iron solution. Combination with arsenic favoured the apparently specific action of the iron, even if arsenic had been previously of no effect. Severe general reactions such as fever, vomiting, pains in the bones, and even an initial aggravation of the condition should not be regarded as an objection to continuing the treatment. According to Weber, the only contra-indications to the treatment are: (*a*) too advanced cases of pernicious anaemia; (*b*) post-nephritic anaemia which shows a tendency to haematuria.

Bowcock reports three cases of pernicious anaemia, in which, after a large number of transfusions, extremely severe reactions occurred in spite of transfusion of apparently compatible blood. In two of the cases the severity of the reaction seemed to have been largely responsible for the patient's death. It was therefore considered inadvisable to continue this form of treatment in the other patient, who died a short time after discharge from hospital. Bowcock considers that the severe reaction was probably due to anaphylaxis and not to haemolysis. He recommends that blood matching should be carried out with the greatest care, and that wherever possible the incubation period should be at least two hours or longer.

Griffin and Szlapka report on 50 cases of pernicious anaemia submitted to splenectomy more than three years ago. The operative mortality was 6 per cent. Ten patients of the remaining 46 survived three years or longer. Five are still living after an average of nearly six years from operation. It is concluded that splenectomy prolonged life in at least 20 per cent. of cases and produced an immediate remission in all who survived operation. There are no particular indications for the operation, which is only advised 'when in view of all the circumstances, personal as well as medical, the possibility of the prolongation of life appeals to the family and to the patient. Occasionally the operation may be performed in order to bring about an immediate remission.'

Leukaemia. According to Sabrazès, acute leukaemia, though a fairly uncommon disease, may occur at all ages, with a special predilection for childhood and adolescence. It is most frequent in the male sex. Various pathological conditions, especially infections, figure in the history, such as rickets, chronic enteritis, haemorrhages, septicaemia, puerperal infection, typhoid fever, scarlatina, tonsillitis, tuberculosis, malaria, syphilis, and influenza. In several cases traumatism has been incriminated. In the splenomegaly, enlargement of the lymphatic glands, and pain on pressure on the sternum the disease may resemble ordinary chronic leukaemia, but the course is more rapid, the tendency to haemorrhages often more marked, the fever high, and the asthenia profound. Bleeding takes place from the mucous membranes of the mouth and gums on the slightest provocation. Acute leukaemia may be mistaken for septicaemia, typhoid fever, dysentery, acute or subacute pulmonary tuberculosis, purpura haemorrhagica, scurvy, acute rheumatism, or acute nephritis. Sometimes the disease is complicated from the first by haemorrhagic and gangrenous processes in the buccal mucosa, gums, or pharynx, and simulates hypertoxic diphtheria or noma. Lastly the disease may be mistaken for acute meningitis owing to meningeal haemorrhages or for urticaria pigmentosa owing to leukaemic lesions in the skin. Treatment of any kind has hitherto proved ineffectual. The measures applicable to chronic leukaemia, such as radium, X-rays, arsenic, and benzol, are inoperative or actually dangerous in acute leukaemia.

Smith reports a case of acute leukaemia in a male infant six weeks old, in whom, according to the history, the disease began definitely at the age of three weeks, while the presence of an axillary node from birth seemed strongly to suggest an intrauterine development of the condition. There were ten or twelve purpuric spots scattered over the body and under the left axilla. On palpation the spleen was felt filling two-thirds of the abdomen. There was slight enlargement of the liver and all the lymph glands. Just before death, which occurred suddenly from pneumonia at the age of two months, the leucocytes numbered 30,000, 2 per cent. of which were polymorphonuclears, 63 per cent. small lymphocytes, and 32 per cent. large lymphocytes. There was no autopsy. The mother's blood picture and white cell count were normal.

Scott, jun., reports a case of lymphatic leukaemia in a child whose first symptoms appeared at the age of 3 years and 9 months, the disease proving fatal two months later from profuse gastric haemorrhage. Blood examination three weeks before death showed 243,000 leucocytes, 97 per cent. of which were lymphocytes. There was much dyspnoea probably owing to the presence of a large thymus, but considerable relief was obtained by X-ray treatment. There was no autopsy apart from examination of the tonsils and adenoids, which showed hyperplasia of the lymphoid elements and no evidence of malignancy or tuberculosis.

Packard and Flood report a case of acute myeloblastic leukaemia in a woman of 26. The earliest sign of onset was a condition of noma, i.e. an ulceration of the mucous membrane of the cheek. The ulceration later spread to the fauces and was found to contain Vincent's spirillum and fusiform bacillus. The authors quote Sondern as finding these organisms in 22 cases. They also mention two cases of leukaemic blood picture in children, in one case lasting five years and in the other seven. Both subsequently showed normal blood. These would appear to have been cases of the 'infective lymphocytosis' of Cabot, and it is interesting to find them classed with true leukaemia, of which the prognosis is thus made to be less unfavourable than heretofore.

Maynard records a case of acute myelogenous leukaemia with only 7,600 leucocytes per c.mm. and 47 per cent. abnormal cells of the myelocyte series. The haemorrhagic diathesis was very evident.

Parkes Weber reports a case of chronic myeloid leukaemia in a man aged 48. During his first stay in hospital he developed a very large haematoma following cupping. His sclerotics became yellow and his urine high-coloured during its absorption. He died soon after his second admission from a huge retroperitoneal haemorrhage, having also developed haematomata on the chest and thigh. The paper gives an account of some similar cases.

Blankenhorn and Goldblatt describe a case of leukaemia in a man aged 40. The particular features of interest were the absence of characteristic blood changes and the presence of classical post-mortem and histological changes. There were skin tumours of a type which has been frequently described. The absence of characteristic blood changes may perhaps have been due to the presence of an abscess in the lung and a septicaemia which allowed of positive cultures from the blood and also from hydrocele fluid. Although the conception of aleukaemic leukaemia seems impossible to some persons, there is no doubt that the tissue changes which necessarily precede those in the blood may be present alone. In such cases the blood changes may never have developed (as in experimental leukaemia) or may have been suppressed by septic changes of later origin—a change which is well attested. It can hardly be said which cause was in operation in this case, but the details and photographs given leave no doubt as to the diagnosis.

Perona reports a case interesting both clinically and pathologically. The patient was a domestic servant aged 31 when first known to be affected with myelaemia. She died ten years later after unusually complete remissions due to X-ray and benzol treatment. The disease terminated with the profuse haemorrhages often seen in the acute form. Following the earliest of these there was a profound change in the blood picture. The white (or at least nucleated) cells were increased, and a large proportion were found to be ‘emocitoblasti’. It would appear that what actually occurred was in the nature of a ‘blood crisis’ such as is seen in many conditions, and there is little warrant for the author’s attempt to set up a new pathological entity ‘erythroblastic leukaemia’.

Symmers describes a case of leukanaemia. There was a leucocytosis of 36,000 and 68 per cent. of mononuclear cells of which most were either myelocytes or at least gave the oxydase reaction. It is unfortunate that in calculating percentages of white cells the author includes 17 per cent. of erythroblasts amongst them. The case appears to have been as typical a case of acute myelaemia as could be described, and Symmers plainly feels that the coincidence of marked changes in the red cells is hardly sufficiently exceptional or unexpected to warrant our classing leukanaemia as a distinct disease entity. He concludes that histogenetically pernicious anaemia, myelogenous leukaemia, and leukanaemia are closely related conditions and represent different quantitative responses on the part of the bone-marrow to regenerative stimuli acting on the myeloblast. Leukanaemia he describes as not a separate disease but one of a group of rapidly progressive derangements of the blood-forming tissues due to infection. He does not appear to attach any particular significance to the anatomical distribution of the lesions or to clinical findings.

Kosmak of New York has collected 12 examples of splenic leukaemia associated with pregnancy, including two cases of his own. The ages of the patients ranged from 24 to 40, the majority being between 32 and 36. All but one were multiparae. A possible hereditary history was mentioned in only one case. In most of the cases the children were born alive and showed no tendency to the disease up to the time of the report, but in a few instances the babies died at periods after labour varying from a few days to five months. The mother survived in only two cases, but for how long was not known. In many cases there was a prodromal period in which pregnancy was followed by progressive emaciation, anaemia, and loss of strength, and during which period the women became pregnant again. Leukaemia therefore did not appear to interfere with conception. Although, judging from the small number of cases on record, leukaemia was a very rare complication of pregnancy, Kosmak is of opinion that a considerable number of cases of marked anaemia in which no satisfactory blood count had been made were probably instances of this disease. The occurrence of pregnancy in leukaemia indicates a most unfavourable outlook for the mother, and pregnancy should not, in Kosmak's opinion, be allowed to take place when the condition is suspected. When the disease is already present abortion seems to be the rule, with a rapidly progressive and fatal course. Owing to the harmful effects which X-rays may have on the foetus, Kosmak recommends that they should not be employed until after the induction of labour.

Rénon and Degrais (1) record a case of pregnancy which occurred during the course of myeloid leukaemia treated by radium. Pregnancy went on to full term, and the mother was delivered of a normal child which was in good health four and a half years later. The absence of myelocytes in the blood of the child at the time of birth was possibly to be explained by the placenta acting as a sort of filter. Another of the writers' patients also became pregnant during treatment, but pregnancy was interrupted at 5½ months.

Wallgren, of Stockholm, records a case of acute leukaemia complicated by gangrenous stomatitis in a primipara aged 29. The slightly macerated foetus which was born in the seventh month showed no leukaemic changes in the organs or the blood. Wallgren regards the fact that acute leukaemia has not been transmitted from the mother to the infant in any recorded case as an argument against the hypothesis that acute leukaemia is a specific infectious disease.

Harris reports a fatal case of polyneuritis in a girl, aged 17, suffering from lymphatic leukaemia. *Post mortem* the spleen was considerably enlarged and soft, and microscopical examination revealed leukaemic infiltration of the liver, nerves, and kidneys with lymphocytes.

According to Howell, leukaemic patients who contract typhoid or paratyphoid infection or are inoculated with typhoid or paratyphoid vaccine may fail to develop the specific agglutinins in the blood. He also found that opsonins are absent in the blood of leukaemic patients after injection of typhoid vaccine. He suggests that this failure of opsonin and agglutinin formation indicates that the tissues of the leukaemic individual have lost the property of antibody formation in general, this loss being due to excessive proliferation of the haematopoietic tissues, one of whose normal functions is the formation of antibodies. Owing to rapidly repeated cell generation the cellular energy used in multiplication prevents the utilization of the energy which is necessary for normal function.

Since 1910 Rénon and Degrais (2) have treated eight patients suffering from leukaemia by applications of radium to the spleen. Although all the patients ultimately died at periods varying from two months to six and a half years after the commencement of treatment, the immediate effects were remarkably good. The spleen, which had occupied the whole of the abdominal cavity, rapidly diminished from day to day and finally resumed its normal size. The number of leucocytes fell from 320,000 to 70,000, then to 20,000, 7,000, and even lower. The myelocytes disappeared, and the number of red cells increased. The general condition improved, the fever subsided, the weight increased by a kilo, and after four to six weeks' treatment a cure seemed to have been effected. The cure, however, was more apparent than real, for from two to eighteen months after cessation of treatment signs of myeloid leukaemia reappeared. Applications of radium were resumed, but with hardly any effect, and death took place in a time varying from two months to six years after the commencement of treatment. The occurrence of the relapse is attributed by the writers to progressive resistance of the myelocytes on which radium can have no further action, whether this be due to habituation of the myelocytes to radium treatment, like that of spirochaetes to arsenic, or to a fibrous change in the leukaemic spleen under the influence of treatment. The writers think that the best way to retard the appearance of relapses and to diminish their gravity is to apply the irradiations less frequently and to make them as intense as possible each time.

Toeniessen discusses the effects on leukaemia obtained from splenectomy, which have, up to now, been unsatisfactory. Of cases recorded to date only one was still quite well after the operation, the greatest proportion having died actually during or immediately after the operation, and others within a few months. Lately, however, there has been a revival in favour of the operation. Lindner, Schilling, Küttner, and others assert that they have had good results. Seefisch and Schilling preceded the operation by X-ray treatment for the purpose of diminishing splenic enlargement and haemorrhages.

One case, described by Delhougue, in which the operation was carried out in the Bonn Hospital, in a woman of 26, was successful, and one and a half years after the operation showed the same fairly normal blood picture as three months after operation.

In view of these good results, Toeniessen communicates a case of chronic myelogenous leukaemia, in which splenectomy exercised a strikingly favourable result for several years. The history of the case is given both before operation in 1909 and up to the beginning of this year. It is that of a man, 37 years of age, who was admitted to hospital in 1909 with abdominal distension, lassitude, emaciation, and palpitation, with pain in the left side. Skin and mucous membranes somewhat pale, abdomen distended; tense, sensitive tumour in the splenic region, otherwise no abnormality found. Wassermann reaction negative. The blood picture was—red cells 6,380,000, leucocytes 38,400, Hb. 65 per cent. No morbid changes in red corpuscles. Under X-ray treatment he improved and was discharged after two months, kept under observation, and was readmitted in May 1910, when the general condition was better than before. The splenic enlargement, however, was somewhat more tense. Pain in the side increased, preventing the patient from going to work, so that splenectomy was decided on.

On June 7, 1910, the spleen, weighing 3 lb., was removed, and when the patient left hospital he was able to walk without difficulty and felt and looked well. The pathological report was that of myelogenous splenic tumour.

From July 1910 to August 1916 nothing was heard of the patient, but according to his own account he felt well and was mobilized in August

1914, and was twice wounded—the second time in the abdomen in March 1916. When in hospital for the latter, the liver was markedly enlarged and very sensitive to pressure; glands also enlarged; albuminuria. Blood as follows: Leucocytes 140,000, red cells 4,600,000, Hb. 80 per cent., polymorphs, 35 per cent., lymphocytes 24 per cent., eosinophils 1 per cent., mast cells 1 per cent., myelocytes 16 per cent.

Patient underwent X-ray treatment and thorium X, and was discharged in May, still with slight pain in the liver, probably due to adhesions. *Blood*: Leucocytes 12,000, red cells 5,200,000, Hb. 105 per cent.; large mononuclears 16 per cent. He served again until 1917, when he was taken prisoner.

The deduction from this case is that splenectomy can be undertaken with benefit in the initial stages of leukaemia, when the general condition is not undermined, and no anaemia or any diminution in blood coagulability exists. The author is also impressed with the idea of X-ray treatment previous to operation, as it induces rapid coagulability.

Haemophilia. Radovici and Iagnov, of Bucharest, report a case of congenital and familial haemophilia in a man aged 33, treated by subcutaneous and intravenous injections of Witte's peptone. Although a complete cure did not result, subcutaneous injections succeeded in accelerating the coagulability of the blood. This effect, however, was only temporary, as twenty-four hours after the injection the coagulation time was just the same as before. Intravenous injections had no effect.

Opitz claims to describe a new syndrome allied to haemophilia. The case was that of a little girl of eight months, born of healthy parents. She had melaena for the first eight days of life, then furunculosis with haemorrhagic staining. When she came under observation she had numerous petechiae on the right knee and shin and on the buccal mucous membrane. On the left thigh was a diffuse tense painful swelling. There was slight enlargement of spleen and liver. The urine contained blood-cells. The Wassermann reaction was negative. Blood showed 77 per cent. haemoglobin, 5,176,000 red cells, 20,800 white cells. Platelets 103,000. There was no clot formation after five hours. The child died, apparently from internal haemorrhage. There was no autopsy.

By examination of the heart blood Opitz concludes that lack of fibrinogen was the cause of this syndrome. This case should be compared with that reported by Rabe and Salomon (vide *Medical Science* 1921, **3**, 398).

Neuffer claims that application of X-rays to the spleen has a most beneficial effect in many cases of haemophilic haemorrhage (by which he appears to mean any otherwise inexplicable bleeding), but is most useful in those in whom the delay in coagulation is least marked. He is unable to explain why the rays act in this way, but points out that the effect is very transitory.

Purpura. Cohen reports six cases of idiopathic purpura in children treated by serum which in four cases was diphtheria antitoxin, in one case the patient's own serum, and in one case the serum of the mother. The doses consisted of 3 or 4 c.cm. given at intervals of three or four days. Five cases recovered and one died. In two cases a relapse of purpura occurred on the supervention of an acute infectious disease—measles in one case and scarlet fever in the other—but was readily cured by further injections of serum. In some of the cases the purpura had persisted for weeks or months without any improvement, so that the disappearance of the eruption after the injections could not be regarded as a mere coincidence. Improvement first set in after the third or fourth injection or about the tenth day, when antibodies begin to appear in the blood after injection of an antigen.

Chalier points out that the chief danger in blood transfusion is that the corpuscles of the donor will be agglutinated and haemolysed by the recipient's serum. It is obvious that this objection is overcome if only serum be transfused. A further guarantee of safety is afforded by the use of serum from members of the same family; this will usually eliminate risks from the transmission of malaria, tuberculosis, &c., which would be known to have occurred if this were actually the case.

The chief indication for human serum therapy is afforded by the opportunity of injecting the seriously ill with serum from convalescents from the same disease, e. g. influenza, typhus, whooping-cough, measles, poliomyelitis, &c. A further indication is afforded by the blood diseases, and it is particularly in haemophilia that Chalier has had excellent results from maternal serotherapy. He has known familial serum efficacious when horse serum had failed to relieve purpura.

Following the work of Chalier and others, Roubier and Richard report a further case of treatment of purpura by injections of human serum. The patient was a woman aged 20, and calcium and peptone injections had no effect. Not until her red cells were so low as 800,000 was serum employed. Her sister acted as donor. Cure was complete.

Dufour and Le Hello have for some time advocated the treatment of rebellious haemorrhage by injection of serum from an animal in a state of anaphylaxis. The present paper summarizes the good results of others with this procedure and records a series of personal cases. The usual route is subcutaneous and the authors see no good reason to adopt the more risky intravenous route.

Grütz describes a case of purpura in which transfusions were done from seven different donors, of whom only two were suitable. The patient nevertheless survived. He goes on to speak of the importance of blood tests and describes his own technique. There is nothing very novel in this except that he advocates direct tests between patient and donor rather than dependance on blood grouping. He approves direct transfusion of whole blood.

Hereditary haemoptysis. Libman and Ottenberg make an interesting addition to the group of haemorrhagic disease and describe as a new syndrome familial hereditary and idiopathic haemoptysis.

Haemoptysis occurred three or four times a year on an average, but did not develop until the age of puberty. From this time it lasted until the end of life. Attacks were sometimes preceded by a 'tickling' feeling two days before, were accompanied by slight fever, and lasted from one to ten days. None were fatal. None of the patients ever showed any signs of tuberculosis. Physical examination revealed nothing abnormal and bronchoscopy was also negative.

In the first generation a single female was known to be affected. She had three children, of whom one male and one female were affected. These three children had altogether 15 children, of whom three males and one female were affected. In the fourth generation there were 32 children; of these none is known to be over 13 years of age and, so far as is known, none have yet developed haemoptysis. The disease is transmitted by either sex, but no unaffected individual has had affected children or grandchildren.

The disease is in many respects comparable with the familial haematuria described by Atlee and Guthrie, and also by Aitken, in the *Lancet* for 1909, a reference not included in the present paper.

Aleukia haemorrhagica. Jerosch prefaces his account of a case by stating that Frank included under the term 'aleukia haemorrhagica' cases of aplastic anaemia, both aregenerative and haemolytic, and regarded it as the initial stage of morbus Werlhofii, for which he gives the synonym 'essential thrombopenia'. The essential features are (*a*) chronic haemorrhagic diathesis, (*b*) a normal red cell count at first, later some diminution with rare nucleated red cells, (*c*) leucopenia with predominance of lymphocytes, (*d*) marked diminution of platelets. Normal coagulation time but increased bleeding time. It may be stated at once that although this syndrome touches at some points the group of cases described by Weil as the endothelio-plasmatic dyscrasia it would appear also to include almost any condition associated with haemorrhage, e.g. leukaemia. Jerosch proceeds to detail at some length a case of leukaemia typical in all particulars excepting only that the total blood count was not increased until towards the end of the disease. So many such cases are now on record, and their affinities are so evident, that Jerosch would appear to strain unduly the bounds even of the wide grouping adopted by Frank.

Polycythaemia. Schulmann and Weismann report a case of polycythaemia of the Vaquez type in a member of a family of which 8 out of 11 children had signs of syphilis, two had died in infancy, and one was not seen. The facies was typical, and ophthalmoscopic examination showed dilated vessels. The red cells reached between eleven and twelve millions. An intensive course of novarsenobenzol produced considerable amelioration, but the red cells were still seven million and the spleen easily palpable.

Laubry and Doumer direct attention to the little-known changes in coagulability of the blood in erythraemia. They have used different methods with apparently conflicting results. Duke's test for the bleeding time was normal. Bloch's test by the addition of calcium to citrated blood required twice as much calcium as usual to cause clotting. By Brissaud's method coagulation did not appear in the normal concentrations. It is obvious that these different tests are open to fallacies and moreover do not call for the same qualities to produce a normal or positive result. Laubry and Doumer discuss the factors likely to be responsible for the variations in this case.

It emerges from their findings and discussion that there is no doubt a failure of clotting in the blood of erythraemics. This may be due to the small ratio of serum to corpuscles compared to the normal, and this view is supported by the facts that defective clotting varies with the red cell count and is found also in the polycythaemia of congenital cardiac lesions. The authors are continuing their observations and will make a further report.

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SYPHILIS

Aetiology. A preliminary report of an experimental study of the **latent syphilitic as a carrier**, by Eberson and Engman, deals with the inactivity of the lymphatic glands, the semen, the blood, the spinal fluid, and the nasal secretion in persons known to have syphilis in a latent form. The inoculation experiments were made on rabbit's testicle. Positive results were obtained from lymphatic glands in three cases and from the semen in two cases. In the latter it is interesting to note that microscopical examination of the semen for *S. pallida* was negative. The blood, spinal fluid, and nasal secretion gave negative results in all cases, including the above cases which were positive for the lymphatic glands and semen. The positive inoculations produced typical syphilitic lesions in the rabbit's testicle containing *S. pallida.* In the positive cases the history of infection was eleven and thirteen years in one gland case and one semen case; one year in two gland cases and one semen case. In one of the positive gland cases the Wassermann reaction had become negative after treatment, and at the time of taking the specimen gave a positive reaction only with cholesterin antigen. A similar case was one with positive semen. These investigations show that persons with a history of old syphilitic infection may harbour virulent spirochaetes for years, in spite of an irregular negative Wassermann reaction or slight positive reactions with cholesterin antigen only.

Riecke and Hoernicke remark that the increased prevalence of venereal disease has led to an increase in **familial syphilis.** They give a detailed account of six instances, all of which came under observation at the Göttingen Clinic in the course of three months.

In the first instance five members of the family were infected; the mother, two children, the maternal grandmother, and an aunt (the father's sister). The father had no signs of syphilis and a negative Wassermann reaction; all the others had signs of secondary syphilis and a positive reaction. The history points to the aunt as having introduced syphilis into the family, and the mode of infection was evidently by buccal contagion, as scars of presumably primary chancres were found in the grandmother and in the younger child. In this instance, therefore, the children were infected with acquired syphilis.

In the second and third instances the father infected his wife, and one or other of them infected their child with acquired syphilis, by kissing or other means.

The fourth instance was one of ordinary syphilitic heredity, where the mother had a positive Wassermann reaction and the eldest child had marked signs of congenital syphilis (Hutchinson's teeth, periosteal nodes, &c.); two younger children had a positive reaction and another child was negative.

The fifth instance was an example of infection of two healthy children, whose father was the first husband of their mother, with acquired syphilis introduced by her second husband. The mother also became infected and gave birth to a child with congenital syphilis by the second husband.

In the sixth instance there was syphilis in three generations. The grandfather had tabes and the grandchild congenital syphilis. But as the mother had undoubted acquired syphilis, the child's infection was evidently direct from her, and not an example of transmission to the third generation.

Lomholt reports three cases of **syphilis acquired by infants during parturition.** In two cases the labour was normal, in the third prolonged. In all cases the chancres were situated on the scalp and were multiple; the occipital glands were enlarged, and *S. pallida* was found in the exudation. Signs of hereditary syphilis were absent, and the Wassermann reaction was negative. In all cases the mothers had condylomata of the vulva, and were probably infected during the last two months of pregnancy. Lomholt draws attention to the rarity of such cases.

Symptomatology. Fischer remarks that with the increased prevalence of syphilis there has been an increase in the number of **extragenital chancres**, many of which are not diagnosed till symptoms of generalized syphilis make their appearance. Among 50 cases which have come under his observation during the last eighteen months he reports one which was situated on the hairy scalp, over the right parietal bone. The glands behind the right ear and angle of the jaw were enlarged. Examination for *S. pallida* was positive and the Wassermann reaction negative. The infection was attributed to an abrasion of the scalp by a hairdresser four weeks previously. Chancres of the scalp are rare, Fournier only having observed three instances in a total of 1,124 extragenital chancres.

Brandt, after pointing out the frequency of 'pseudo-reinfections' since the introduction of salvarsan, consisting of chancriform papules which are mistaken for new chancres, reports a case which he considers one of true **reinfection.** The patient, a prostitute, was treated in Neumann's Clinic in 1902 for chancre of the cervix and secondary syphilis. After 18 inunctions of mercury the signs disappeared. In 1918, 16 years after the first infection, she presented a typical syphilitic chancre of the vulva with a negative Wassermann reaction. A week later the latter became positive and spirochaetes were found in the chancre. Later on papular syphilides appeared. The author draws attention to the disappearance of the symptoms of the first infection after incomplete treatment by only 18 inunctions. He also mentions that the possibility of superinfection, shown by the investigations of Finger and Neisser, must be always borne in mind in such cases.

Pontoppidan records the case of a manufacturer, aged 57, who was treated in 1889 for a chancre and adenitis, with mercurial inunctions. Owing to relapses, this treatment was repeated 3 months later, half a year later, and again in 1891, 1896, and 1897. The patient showed no further signs till 1918, when, at his own urgent request, a small pedunculated, papillomatous tumour, situated on the pubic region for 3 years, was removed.

After its removal, its base was painted with chromic acid to arrest slight haemorrhage. Eight days later it was covered by a crust and seemed to be healing, but a month later a dirty ulcer, of the size of a small coin, had developed. It continued to grow larger in spite of treatment with silver nitrate and other remedies, and, epithelioma being diagnosed, X-ray treatment was prescribed. Only temporary improvement was effected, and when the ulceration began to extend further and to be associated with severe pain, X-ray dermatitis was diagnosed, and the progress of the ulceration was regarded as an X-ray reaction. Several months after the onset of the symptoms, the ulcer measured 3½ by 7½ cm., the patient felt very ill and depressed. and complained of severe pain, headache, and fever. It was not till superficial, crust-covered ulcers developed in various other parts of the body, and painful superficial serpigenous ulcers appeared on the fauces, that syphilis was suspected. Within 3 weeks of the institution of treatment with potassium iodide the ulcers had completely healed, and the patient again felt perfectly well. The Wassermann reaction was positive. The appearance of the scars left by the healed ulcers was typical of tertiary syphilides.

Meincke records the case of a man, aged 30, with patches of syphilides on both cheeks and on both thighs. There was also a semi-circular patch on his forehead, extending from one eyebrow to the other. This condition had developed in the course of 6 to 8 weeks. A white scar was still demonstrable on his penis, the remains of a chancre which had developed 12 years earlier. He had never been treated for syphilis. The Wassermann reaction was negative. It was still negative after 12 inunctions with mercury which diminished the syphilides without altogether banishing them. Even after further treatment with mercury and neosalvarsan, the Wassermann reaction remained negative.

Visceral syphilis. Wile (1) (2) (3) gives a résumé of our knowledge of syphilis of the liver, kidney, and stomach, together with his own experience. That many cases of *hepatic syphilis* are not recognized during life is shown by McCrae's statistics, showing a diagnosis of 0·2 per cent. of tertiary syphilis of the liver in 27,000 general medical cases, and a post-mortem finding of 1·5 per cent. in 3,300 autopsies. Wile found less than 1 per cent. of icterus in secondary syphilis, the majority of cases being mild and due to obstructive jaundice. Severe icterus, or syphilotoxic parenchymatous hepatitis, constituting one form of acute yellow atrophy, is rare and usually fatal; but Wile had a case which recovered under intensive antisyphilitic treatment, and he considers the prognosis better than in cases of acute yellow atrophy due to other causes. With regard to the interstitial hepatitis of tertiary syphilis, Wile found no evidence of alcoholism in his cases, an association which other authors have said to be frequent.

Gumma of the liver, if small, may cause no symptoms, but larger gummata give rise to a nodular surface of the liver. Gumma is often associated with interstitial hepatitis. The diagnosis of hepatic tertiary syphilis is difficult in the absence of other signs of syphilis. Small size of the liver, absence of jaundice, and gastro-intestinal symptoms are suggestive of syphilis. A nodular surface of the liver may be mistaken for carcinoma, but the carcinomatous nodules are of more rapid growth. The Wassermann test is of assistance, but syphilis and carcinoma may occur together. Ascites and jaundice are said to be more common with carcinoma, and fixation of the liver during respiration by adhesions more frequent with syphilis. Wile points out that ascites in syphilitic cirrhosis often increases after treatment, owing to the formation of more cicatricial tissue.

With regard to *renal syphilis*, Wile states that in the acute parenchymatous nephritis of secondary syphilis both intensive mercurial and arsenical treatment are beneficial, but that in chronic interstitial nephritis due to late syphilis treatment has little effect. Gumma of the kidney is rare, and usually only discovered at autopsy or at operation for some other supposed condition, such as tuberculosis or new growth.

A few cases of *syphilitic pyelitis* have been recorded in which the pelvis of the kidney alone appeared to be affected, and these recovered with antisyphilitic treatment. Syphilis of the *ureter* seems to be rare; a case in which the ureter was obstructed by a gummatous growth was reported some time ago by Hodden. With regard to the *suprarenals*, Wile remarks that syphilis should be looked for in all cases of suprarenal insufficiency with characteristic low blood-pressure and debility. Some cases with signs of Addison's disease are said to have improved under antisyphilitic treatment. The same with cases of *paroxysmal haemoglobinuria*, the majority of which appear to be due to acquired or congenital syphilis.

Syphilis of the stomach is regarded by Wile as more common than is generally supposed. In early syphilis he distinguishes between indirect gastric symptoms—vomiting in cerebral syphilis and anorexia in the fever of secondary syphilis—and direct symptoms due to gastric catarrh. The latter, he thinks, may be due to an erythematous eruption, with or without erosion of the mucous membrane, corresponding to the early secondary skin eruptions. In the rare cases which have come to autopsy, erosions have been reported. Late gastric syphilis is divided by Wile into gastric and perigastric, the former including catarrh, round ulcer, submucous gumma, diffuse infiltration, and cicatrices; perigastric syphilis consisting of involvement of the omentum, mesentery, and retroperitoneum. Syphilitic catarrh, characterized by resistance to the usual remedies and responsive to antisyphilitic treatment, is probably an early stage of the more severe forms. The proportion of round ulcers of the stomach due to syphilis has been variously estimated at from 1 to 20 per cent. by different authors. Wile favours a low percentage. The only sign differentiating syphilitic from ordinary round ulcer is said to be diminished acidity of the stomach contents. Most cases react well to antisyphilitic treatment. Wile mentions one case in which the Wassermann reaction was negative, but *S. pallida* was found in the excised ulcer. Submucous gummas form the majority of cases of gastric syphilis and are difficult to diagnose from carcinoma, especially when associated with gummatous swellings of the liver, which may be mistaken for metastatic carcinomatous nodules. Diffuse syphilitic infiltration of the stomach, leading to distortion and hour-glass stomach, is more benign than the other forms. Contraction and distortion with strong peristalsis, shown by X-ray examination, is said to be suggestive of syphilis. Syphilitic lesions situated at the pylorus may cause stenosis from scar formation.

The chief difficulty in the diagnosis of syphilis of the stomach is carcinoma, which is often associated with it and may very probably develop from syphilitic scar tissue. In all cases the therapeutic test should be applied.

The relation of syphilis to *cancer of the buccal cavity* has been investigated by Cary, by clinical and serological examination. Evidence of syphilis was found only in 6·23 per cent. of 721 cases of cancer of the lips, tongue, and mouth. The incidence was highest in cancer of the tongue, 14·5 per cent., a much lower figure than that found by other observers. Very few cases were found to follow leucoplakia. Cary warns against too prolonged antisyphilitic treatment in the presence of a neoplastic growth.

Owen has investigated the *aetiological factor of syphilis in cirrhosis of the liver.* In 19 cases of atrophic, nodular, or 'alcoholic' cirrhosis he found evidence of syphilis in 7, an alcoholic history in 6, and both combined in 4 cases. He concludes that the frequent association of syphilis with hepatic cirrhosis indicates that it is an aetiological factor, especially when combined with alcohol; but he admits that cirrhosis of the liver may also be produced by other chronic infectious processes.

Cardio-vascular syphilis. Sternberg, discussing syphilis of the circulatory system, distinguishes between specific and non-specific lesions. The former consist of a primary progressive affection of the vessel walls, the latter include thrombi, infarcts, necrosis, myomalacia, reactive new tissue formation, and atheroma, which is often a secondary complication of arterial syphilis. Clinically and anatomically there are several morbid conditions which are characteristic of syphilis, and which are often combined, such as aortitis, aortic aneurysm, and aortic incompetence. Syphilitic aortic incompetence causes less hypertrophy of the left ventricle than endocarditic incompetence, because the coronary arteries are generally affected and hence the heart-muscle is less nourished. Syphilitic disease, however, is often combined with endocarditis due to other causes. Angina pectoris is often due to syphilis of the coronary arteries. Syphilitic asthma, manifested by nocturnal attacks similar to bronchial asthma, may be due to gummatous myocarditis. Rosenfeld found gummata in the heart-muscle in two cases. A form of pericarditis, named by Kernig *pericarditis epistenocardiaca,* is an acute inflammation of the pericardium following stenocardia, and is due to thrombosis in a branch of the coronary vein, forming the so-called myomalacial focus in the heart-muscle which gives rise to inflammatory reaction. If this reaches the pericardium it causes pericarditis. Sternberg describes a form of chronic partial cardiac aneurysm associated with pericarditis epistenocardiaca and angina pectoris. In this condition syphilitic arteritis leads to myomalacia of the whole thickness of the heart wall, and the resulting cicatrix gradually yields and forms a cardiac aneurysm. Such cases tend to a fatal termination from rupture or cardiac insufficiency. Disturbances of the cardiac rhythm may also be caused by syphilis. There is a positive Wassermann reaction in 40 per cent. of cases of the Adams-Stokes symptom complex, and gummata or cicatrices have been found in the heart. Other syphilitic lesions mentioned by Sternberg are intravalvular aneurysm of the sinus of Valsalva with aortic incompetence (Kraus); *livedo marmorata racemosa* due to syphilis of the small cutaneous arteries (Ehrmann); syphilitic phlebitis, which is a frequent cause of thrombosis.

Regarding the pathological distinction between syphilitic disease of the vessels and non-syphilitic athero-sclerosis, Sternberg remarks that this is easy in extreme cases, but that calcification and fatty changes often occur in syphilitic arteritis which are difficult or even impossible to distinguish from those of non-syphilitic athero-sclerosis. Microscopic examination is not always conclusive; finally, athero-sclerosis may be superimposed on syphilitic arteritis. Diagnosis depends on examination for *S. pallida,* the Wassermann reaction, and other signs of syphilis.

With regard to treatment, pathological anatomy shows that healing of vascular syphilis may occur naturally. Specific treatment influences the tissue changes, but not the sequelae, such as severe myomalacia and aortic aneurysm.

Sternberg points out that a definite scheme of antisyphilitic treatment cannot be formulated and that each case must be treated individually. Early diagnosis is essential. Iodides, mercury, and salvarsan, in cautious doses, may do much good in aortitis and angina pectoris, and the size of aortic aneurysms may even be diminished. Good effects may be attained in cases with no evidence of syphilis; hence antisyphilitic treatment is indicated in cases of doubtful diagnosis. In all cases, however, the immediate results must be distinguished from the permanent, which are always doubtful, especially in the case of cerebral arteritis.

Writing on the same subject, Rosin recommends the following treatment for cardiac and vascular syphilis: (1) large doses of iodides continued for years with intervals, preferably sodium iodide, and given in gelatine capsules or per rectum if it is not well borne by the stomach; (2) energetic treatment by inunction or injections, except in cases of granular kidney; (3) salvarsan after or concurrently with mercury. This treatment should be repeated once a year at least till symptoms disappear or the Wassermann reaction becomes negative, and should be controlled every six months by an X-ray examination and estimation of the blood-pressure. In neurosyphilis caution is necessary and small doses (0·2 gm.) of neosalvarsan should be given weekly. Cases of hypertension require nitroglycerine in addition to antisyphilitic treatment; other nitrites are not so suitable, and amyl nitrite is dangerous. Nitroglycerine is best given in ½ mgm. doses in an alcoholic solution, which is preferable to tablets. This dose is given 3 to 5 times daily for several weeks till the blood-pressure is lowered. It may have to be repeated for years. Nitroglycerine is also indicated in angina pectoris and cerebral phenomena, but not in advanced kidney disease.

Reid, writing on *syphilitic aortitis,* points out the extreme variation in the date of onset of symptoms—from six months to 33 years in his cases. He mentions a case in which death occurred from perforation of the aorta in early secondary syphilis (Brooks), and one of aneurysm of the coronary artery at 18 months (Osler). In 41 cases observed by Reid *S. pallida* was found in 11. In 54 autopsies the first part of the aorta was affected in 94 per cent., the coronary arteries were normal in 27, there was slight fibrosis in 15, stenosis of the orifice in 8, and occlusion in 4. The aortic valves were affected in 41 cases, in 14 there was incompetence, in one stenosis, in 9 the bases of the valves were adherent.

In 61 cases observed clinically the symptoms were praecordial pain and pain in the chest, arms, and shoulders, and dyspnoea. The physical signs were a diastolic murmur in 23, diastolic and systolic murmurs in 20, a systolic murmur in the aortic area in 19, a systolic murmur in the aortic area and at the apex in 7, a systolic murmur at the apex in two. The heart was enlarged to the left in 29, downward to the sixth interspace in 16. Other symptoms were Corrigan's pulse in 9 cases, a systolic thrill in the aortic area in two cases, and pulsus alternans in two cases. The Wassermann reaction was frequently negative, and mention is made of Warthin's researches, in which *S. pallida* was found in the aorta or myocardium in cases which had a negative Wassermann reaction during life.

For diagnosis Reid considers that radioscopy gives the best evidence, but is not to be relied upon in early cases. The chief differential diagnosis has to be made from rheumatic aortitis, which, according to Reid, may even cause aneurysm. Aortitis has also been reported in cases of infective fevers and in gonorrhoea. Non-syphilitic aortitis, however, is rare. Aortic insufficiency has been stated to be due to syphilis in 81 per cent. of cases. Mitral lesions are usually of rheumatic origin.

As regards treatment, Reid gives alternate courses of mercury and diarsenol, 0·15 to 0·45 gm. Iodides he considers to be less effective. He also advises antisyphilitic treatment in doubtful cases, and regards the therapeutic test as of more value than the Wassermann reaction. Every case of cardiac disorder of obscure origin, especially in a young adult, should suggest syphilis.

A remarkable case of *rupture of a papillary muscle of the heart* due to syphilis is reported by Spalding and von Glahn in a man aged 31. The symptoms were those of cardiac enlargement and a positive Wassermann reaction, followed by cardiac dilatation and failure. The autopsy showed syphilitic aortitis and aortic regurgitation, fibrous myocarditis, cardiac hypertrophy, and dilatation and necrosis and rupture of the posterior mitral papillary muscle. Spirochaetes were found in the latter beyond the necrotic area. Histological examination showed coagulative necrosis, but no epithelioid, giant, or plasma cells characteristic of gumma.

Pautrier and Roederer report a case of *syphilitic phlebitis* affecting both internal saphenous and both external saphenous veins, and appearing one month after the chancre. They mention the absence of severe symptoms, such as oedema and embolism, and attribute the latter to the fact that the phlebitis is subendothelial and does not effect the endothelium. They consider syphilitic phlebitis to be more common than is usually supposed, and that it is sometimes mistaken for lymphangitis.

Diagnosis. Warthin and Starry describe an improvement of their *silver-agar cover-glass method of staining Spirochaeta pallida* in sections. The sections of tissue, which have been fixed in neutral formaldehyde and embedded in paraffin, are mounted on cover-glasses with albumin fixative, and, after removal of paraffin by xylol, alcohol, and water, are rinsed with 2 per cent. silver nitrate, covered with a second cover-glass, and placed in a bottle of the same solution, which is placed in an incubator for half an hour or an hour. They are then removed and the cover-glasses separated. The cover-glass with the section is then placed in the following reducing mixture:

2 per cent. silver nitrate solution	3 c.cm.
Warm glycerine	5 c.cm.
Warm 10 per cent. aqueous gelatin solution	5 c.cm.
Warm 1·5 per cent. agar suspension	5 c.cm.
5 per cent. aqueous hydroquinone solution	2 c.cm.

After the section is reduced it is rinsed in 5 per cent. sodium hyposulphite solution, then in distilled water, and mounted in balsam.

The silver solution should always be freshly made, and the silver impregnation should be carried out in dark bottles. The authors find that the second cover-glass is essential, and that good results are not obtained when the sections are left uncovered. The success of the method also depends on the reduction process. This can be controlled by varying the amount of hydroquinone and also the temperature. The advantages of this method over the original Levaditi method are its rapidity and its applicability to single sections.

The frequency of *mixed chancre* and its bearing on the early diagnosis and treatment of syphilis is discussed by Belgodère. He quotes Payenville's figure of 25 per cent. for chancres with double infection. Out of 267 chancres examined by Belgodère no less than 125 are said to be chancroids, 73 syphilitic, 17 mixed infection, and 52 negative, according to bacteriological examination. The methods of staining used were carbol thionin for the bacillus of Ducrey, and the Fontana-Tribondeau method for *Spirochaeta pallida.* According to Belgodère the latter gives as good results as the dark ground method, and has the advantage of making permanent preparations which can be referred to. By this method he obtained 85 per cent. positive results in syphilitic chancres, whether old or new, treated or untreated. The carbol thionin stain gave 81 per cent. positive results in all cases of soft chancre, and 100 per cent. in early untreated cases—a higher figure than that generally supposed to be attainable.

In mixed chancre Ducrey's bacillus and the spirochaete were not always found simultaneously. The former was often present alone in sores having the clinical appearance of chancroids; later on, when the characters became more suggestive of syphilis, the spirochaete was found, while Ducrey's bacillus had disappeared. In one case a triple infection of gonococcus, Ducrey's bacillus, and the spirochaete was observed.

From their experience of the *Wassermann reaction,* Nicolas and Gaté come to the following conclusions: (1) a negative reaction cannot eliminate syphilis and should always be followed by a careful clinical examination and a therapeutic test; (2) a positive reaction which is contradictory to the clinical evidence should always be repeated in a few days, and if the second test is again positive the final decision should rest with the clinical evidence. The authors regard the diagnostic value of the Wassermann reaction as very limited and not to be depended upon in medico-legal questions, life assurance, or the question of marriage. They point out that while remarkable evidence of certain infections may be given by the discovery of antibodies and other substances in the serum, when we are concerned with a non-specific reaction such as the Wassermann the results must always be open to question. Laboratory tests are useful aids, but the clinical diagnosis must remain predominant.

A preliminary report on the study of the occurrence of a *positive Wassermann reaction in non-syphilitic patients* after arsenical treatment, carried out at Jefferson Medical College, is issued by Strickler, Munson, and Sidlick. The common observation that many syphilitic patients clinically cured gave positive reactions in spite of energetic arsenical treatment suggested the idea that some of these positive reactions might be caused by the drug itself. To investigate this problem, 30 patients suffering from various non-syphilitic skin affections, with a negative Wassermann reaction and no history of syphilis, were selected. These were treated with weekly injections of 0·5 gm. arsphenamine. Of the 30 cases, 9 gave a +2 or greater degree of positive reaction; 5 gave a +1 positive reaction; 2 gave a doubtful result, and 8 were negative. In a few cases the positive result persisted after cessation of arsenical treatment. Thus 38 per cent. gave a degree of inhibition of haemolysis (50 per cent. or +2) which is usually regarded as indicative of syphilis.

Against the possibility of these results being of the nature of provocative reactions are: the negative evidence of syphilis, the absence of therapeutic effect on the skin lesions, and the fact that most of the cases changed from negative to positive after a much longer interval than in the provocative test. The authors are inclined to attribute the results to the arsphenamin itself, more especially as the positive reactions occurred more often in patients who suffered from the effects of this drug. In support of this view they mention the observations of Strathy and others on delayed arsenical poisoning (see *Medical Science*, 1921, **3**, 309), and suggest that, as the result of the action of arsenic, the liver, spleen, and bone-marrow may form a lipoidal substance which, when in sufficient quantity in the blood, is capable of causing a positive complement-fixation reaction. Whether this lipoidal substance is analogous to that resulting from the action of *S. pallida* it is imposible at present to decide, but chemical research is being conducted with a view to elucidate this question.

The following suggestions as to the bearing of their results on the diagnosis, prognosis, and treatment of syphilis are made by the authors. As regards diagnosis, a positive complement-fixation reaction for syphilis obtained with the serum of a patient treated with arsphenamine for a non-syphilitic disease should be interpreted with great caution, and a diagnosis of syphilis should not be made hastily or dogmatically.

As regards treatment, they are of opinion that sometimes too much arsenic is administered in the treatment of syphilis, and that this drug may sometimes be responsible for the persistence of a positive Wassermann reaction. The hope of a rapid and radical cure of syphilis, or 'therapia sterilisans magna', has not been realized. The authors recommend a reduction in the total amount of arsphenamine, and the thorough and early use of mercury. They favour the method of three or four intravenous injections of arsphenamine given at intervals of one or two days, instead of eight to ten injections given at weekly intervals. By this method of attacking syphilis with smaller doses of arsphenamine at shorter intervals and pushing mercury to a greater degree, they think the number of persistently positive Wassermann reactions will be reduced.

With regard to *prognosis* and *curability*, the authors draw attention to the tendency of serologists to make the Wassermann test increasingly sensitive, and the question whether a clinically cured patient should be treated till he is serologically negative. They mention the observations of Wile, who showed that in patients in the same stage of syphilis, treated under similar conditions and by the same method, the percentage of cures varied with the technique of the Wassermann test employed, and agree with him that 'in the presence of intensive therapy, a positive test does not necessarily mean living spirochaetes and potential syphilis any more than a positive tuberculosis test in an individual who has had tuberculosis would indicate the presence of living tubercle bacilli'.

They conclude that, in our present ignorance of the nature of this reaction, and in the light which their study throws on the interpretation of some persistent positive reactions, serological and clinical cures are not necessarily parallel. Energetic treatment attempting to render a persistently positive reaction negative may be not only useless but also misdirected.

Stern, writing on the occurrence of a positive Wassermann reaction in non-syphilitic diseases, reports a case of sarcoma of the cerebellum in a malarial subject in whom the blood gave a positive reaction of one degree, and the cerebrospinal fluid a positive reaction of three degrees. The patient died and no signs of syphilis were found. The reaction could not be explained by pleocytosis, which was absent, nor by the formation of lipoid substances from degeneration of the tumour, the latter being small and showing no such changes. Stern mentions reported cases of tuberculous meningitis in which the cerebrospinal fluid gave a positive Wassermann reaction, and suggests further research on the presence of this reaction in non-syphilitic conditions. Plaut explained the occurrence of positive reactions in cases of tuberculous meningitis by the passage of the substances causing the reaction from the blood to the cerebrospinal fluid, owing to increased permeability of the meninges, and assumed that such cases were tuberculous meningitis occurring in a syphilitic subject. Fildes and Parnell also consider that the complement binding substances in the cerebrospinal fluid are derived partly from the blood, but attribute positive reactions in non-syphilitic meningitis (tuberculous or meningococcal) to the use of unheated cerebrospinal fluid in the test.

As the result of a series of observations on the diagnostic value of the *colloidal gold test*, Thompson finds that the so-called 'paretic curve' is not confined to cases of general paralysis, but occurs in nearly 50 per cent. of cases of cerebrospinal syphilis. Hence the presence of a paretic curve does not differentiate between general paralysis and other forms of cerebrospinal syphilis, but its absence points to the latter. Thompson also states that the paretic curve is common in multiple sclerosis, and may also occur in tabes, tuberculous meningitis, brain tumours, Korsakoff's psychosis, epilepsy, eclampsia, and in some drug intoxications, such as lead poisoning. He thinks that the paretic curve indicates more or less destruction of nerve-cells and points to parenchymatous involvement of the brain, while the milder gold curves occur in meningeal and vascular lesions. Under intensive treatment he found that the paretic curve may become irregular and more of the syphilitic type, and finally negative. On the other hand, it may become more pronounced after treatment, even when previously negative, being thus apparently of the nature of a provocative reaction.

Prophylaxis. The prophylaxis of syphilis by arsphenamine is advocated by Michel and Goodman, who have employed it in 30 patients, most of whom were known to have had connexion with syphilitic women. The doses (arsphenamine) averaged 0·3 gm., the number of injections three, and the intervals between injections from two to five days. The patients were under observation long enough to pass the limit of the primary incubation period, and none of them developed a positive Wassermann reaction. In support of this procedure the authors quote the experiences of other observers. Thus, Fournier and Guinot treated 40 women who had had connexion with men having syphilitic lesions of the genitals; all the women had negative Wassermann reactions and no signs of previous infection. None of them developed syphilis, but five other women, similarly exposed, who refused treatment, developed the disease. Lacapère and Laurent reported the cases of three officers who had connexion with a woman in the active stage of syphilis; two received a dose of salvarsan and remained uninfected, while the third, who refused the injection, developed a chancre. Also, the case of a man with erosive syphilitic lesions of the penis, who had daily connexion for 15 days with a woman presenting no sign of syphilis, no history of antecedent syphilis, and a negative Wassermann reaction. She was given eight injections of neosalvarsan and remained free from infection. Michel and Goodman have failed to discover any report of the failure of these prophylactic injections when made in the incubation period of syphilis. They consider that this procedure, in spite of the objections raised against it, fills a place in the prophylaxis of syphilis.

Treatment. The possibility of *aborting syphilis* by early and energetic treatment, although difficult of proof, has some evidence in its favour. Many cases have been reported in which no further symptoms occurred and the Wassermann reaction never became positive, when treatment was commenced during the negative stage of the primary period. The only proof of cure, however, is the occurrence of reinfection, and unfortunately the majority of cases reported as examples of reinfection were in all probability only instances of recurrent lesions.

This question has been studied by Lévy-Bing and Gerbay, who arrive at the conclusion that syphilis can be aborted by arsenical treatment commenced before the 38th day after the date of infection. From serological examinations carried out during primary syphilis they regard this date as the critical time when, in untreated cases, the Wassermann reaction first becomes positive. The 38th day is not an absolute date, since the critical period has a duration of about eight days, but it represents the limit beyond which abortive treatment becomes less probable of achievement. According to these observers, if treatment is commenced before this date the Wassermann reaction remains negative, or at any rate feebly positive; if commenced after this date it becomes distinctly positive.

In support of this view two cases are reported. In the first case the chancre was seen 24 hours after its first appearance, 25 days after infection; Wassermann and Hecht reactions negative; *S. pallida* positive. Intravenous injections of sulpharsenol were commenced at once, 12 injections being given in 34 days in doses of 0·06 up to 0·42 gm. The serum reactions remained negative while under observation for seven months, and the cerebrospinal fluid was also negative. In the second case the treatment was commenced by an injection of neosalvarsan 35 days after infection, followed by a course of intravenous injections of sulpharsenol and intramuscular injections of benzoate of mercury. The serum remained negative for five months, and the cerebrospinal fluid was negative six months after the appearance of the chancre.

Scholtz, writing on the *indications for salvarsan treatment*, remarks that the more widely salvarsan is used the more lax are the indications. Many think that every positive Wassermann reaction and every genital ulcer are indications for salvarsan, and some even advise prophylactic treatment with this drug after a coitus with a person suspected of syphilis (see above). Scholtz does not approve of such indiscriminate measures, and urges that the use of salvarsan should be individualized and not subjected to hard and fast rules. The organs affected, the constitution and habits of the patient, should all be considered. The indications for salvarsan must be limited by general principles.

With regard to the mode of action of salvarsan, Scholtz holds that it is spirochaeticidal, while mercury and iodides act chiefly on the affected tissues; but mercury, he thinks, may act as an antitoxin to the spirochaetal toxin. Iodides he believes to have an influence on the Wassermann reaction, which generally becomes negative after 100 to 150 gm. Although the mode of action of mercury and salvarsan is different, syphilitic lesions disappear under either, but generally more rapidly with salvarsan. Mercury and iodides are sufficient for symptomatic treatment, but this is not the case with regard to infectivity, the period of which is reduced more rapidly by salvarsan.

To compare the effects of mercury and salvarsan on the results and general course of the disease, Scholtz investigated one series of cases treated by mercury alone and another series treated by mercury combined with salvarsan. In 250 cases, examined from 5 to 20 years after infection, which had been treated with mercury only, 63 per cent. were regarded as uncured. Comparing patients who came under observation 5 to 10 years after infection with those who came 10 to 20 years afterwards, the latter group showed a higher percentage of negative Wassermann reactions. With regard to the effect of the nature and duration of mercurial treatment, it was found that after one course of mercury the uncured were 80 per cent., after two or more courses 50 per cent. No difference was found between symptomatic and chronic intermittent treatment as regards the results.

With combined mercurial and salvarsan treatment in the early stages much better results were found. The fate of the first hundred cases treated by the combined method between 1911 and 1913 was followed. Of these 90 per cent. were clinically cured and had a negative Wassermann reaction, 10 per cent. were regarded as uncured, but in some the only evidence was a positive reaction. About 80 per cent. had had only one course of treatment. The course regarded by Scholtz as sufficient consisted in 6 weekly injections of salvarsan (0·3 gm.) in primary, and 8 injections in secondary syphilis, with mercury simultaneously. With salvarsan alone, especially in secondary syphilis, the results were not so good even with 10 to 15 weekly injections, and severe neuro-recurrences sometimes occurred. The superiority of the combined treatment over pure salvarsan treatment is not easy to explain, but Scholtz thinks it may be due to the antitoxic action of the mercury already mentioned. After the third year of syphilis the combined treatment is less effective, and repeated courses are required. After the fifth or sixth year the Wassermann reaction may often be kept negative by iodides, and mercury and salvarsan are not so necessary. Insufficient treatment by the combined method is inferior to treatment by mercury alone. In 100 cases of this kind, previously treated more or less intensely with mercury, but with only 2 to 5 injections of salvarsan, only 23 were cured clinically and serologically.

The indications, therefore, for salvarsan are summed up by Scholtz as follows:

(1) In the early stages, provided the age and constitution of the patient allow it, an intensive course of salvarsan with mercury, or two or three milder courses of 2 or 3 injections at short intervals. Otherwise salvarsan is best left alone. If the treatment has to be interrupted owing to side-effects of salvarsan, mercury should be continued longer.

(2) Salvarsan is not indicated in doubtful cases or before the diagnosis is certain. Prophylactic injection before any sore has developed is not indicated, because it requires an intensive course, and also because it is not certain whether the disease is more easily cured at this period than after the primary sore has appeared. Lesser's extravagant claim that syphilis can be aborted in 100 per cent. of cases in the primary negative stage by three injections of neosalvarsan is not supported by Scholtz.

(3) In primary syphilis with a negative Wassermann reaction one intensive course is sufficient. In primary syphilis with a positive reaction and in secondary syphilis, a second milder course should be given after an

interval of six to eight weeks. In the fourth or fifth year after infection salvarsan should only be given to young and strong subjects, not to women and old people. In the later stages iodides should be given.

(4) In tabes salvarsan is only indicated in progressive cases, and to relieve the pains and crises. If improving, a second and third course should be given. In general paralysis, Scholtz does not think much can be done even by intraspinal treatment.

(5) After an experience of more than a year with silver-salvarsan, Scholtz comes to the conclusion that it is inferior to the old salvarsan and not less likely to be followed by severe side-effects such as encephalitis, dermatitis, and neuro-recurrences.

MacCormac and Kennaway, having found that the Wassermann reaction often became positive after the usual course of treatment by intravenous injections of novarsenobillon and mercury, have modified this course both by increasing the number of injections and the doses. The scheme they now adopt consists of ten intravenous injections of N.A.B. at weekly intervals, the first dose being 0·6 gm., the rest 0·9 gm. These doses were found not to be excessive. One series of cases was treated without, and another with, simultaneous weekly injections of mercury, the results on the Wassermann reaction being slightly in favour of the combined treatment. A noteworthy point is that, by making weekly blood tests in cases of primary syphilis with negative reactions, it was found that the reaction often became positive during treatment; hence it was concluded that no distinction should be made between primary cases with negative and those with positive reactions. This scheme of treatment is continued by intramuscular injections of mercury for three months. If the Wassermann reaction is then positive the whole course is repeated. If negative, mercury is continued in the form of pills or injections for two years, the blood being tested every three months. By the adoption of this scheme of treatment the authors found considerable diminution in the subsequent clinical and serological relapses.

In tertiary syphilis, however, they found that treatment had little or no effect on the blood reaction, the original positive or negative reaction remaining constant.

Corraz also found that there is no essential difference between primary negative and primary positive syphilis. In 11 cases of primary syphilis with negative Wassermann reaction he found, by weekly tests, that all but two became positive during treatment with novarsenobillon. He mentions that the same conclusion was obtained by Gouin and Leblanc, who found that only one case out of 12 remained negative.

Minet reports further experiences with *daily subcutaneous injections of novarsenobenzol.* He finds the best vehicle a 4·7 per cent. solution of glucose, by means of which local reaction and discomfort appear to be reduced to a minimum. Oily suspensions, he finds, give rise to severe local reactions and painful nodosities, and the addition of novocain, while diminishing the immediate pain, appears to increase the later pain and reactions. The course he gives consists in 15 daily injections; the usual dose 15 cgm., occasionally 30 to 45 cgm. The courses are repeated monthly, so that from 20 to 30 gm. of novarsenobenzol are administered in the course of a year. Good results are claimed by this method in secondary and tertiary syphilis, and also in tabes. Mercury was given concurrently. In preparing the injection, rapidity is essential so as to avoid exposure to air.

The injections are made in the upper third of the thigh and placed in contact with the fascia lata.

Gutmann reports on Linser's method of intravenous injection of *a mixture of salvarsan and mercury perchloride.* The doses of the perchloride were from 0·01 to 0·02 gm. The course consisted of 11 to 13 injections at intervals of two days. In six or seven weeks a total of 4·5 to 5·4 gm. of neosalvarsan and 0·18 to 0·22 gm. of perchloride were administered. The therapeutic results were good, but the effect on the Wassermann reaction was not so favourable.

Rothman, as the result of experimental research with solutions of salvarsan and perchloride of mercury, concludes that the perchloride in Linser's mixture is first reduced to the subchloride and then to metallic mercury in a colloidal state by the reducing action of the salvarsan, which is itself probably in a semi-colloidal state. He thinks that any oxidation of the salvarsan is insignificant.

Lenzmann claims to have obtained good effects by combined treatment with *silver-sodium salvarsan and colloidal silver.* The former was given in doses of 0·05 gm. daily for four days followed by an interval of four days, up to a total of 16 to 20 injections. Collargol in doses of 0·05 to 0·1 gm. was given simultaneously.

The treatment of syphilis by *fumigation,* a method which has for some time been discarded, was revived during the war by Burns, who employed it at No. 5 General Hospital, New York. The preparation used appears to have been first tried by Lewengood, of New York, who obtained it from a lay source, and, after making improvements on it, gave it the name of 'spirocide'. Analysis showed that a dose of 10 gm. contained 23 per cent. metallic mercury, 22·5 per cent. copper sulphate, 9·8 per cent. ferric oxide. 9·3 per cent. combined potassium, 2·3 per cent. calcium carbonate, 2 per cent. glucose, 34 per cent. vegetable matter, 19 per cent. water, and 2 per cent. sand. The patient is covered with a sheet and allowed to inhale the vapour till the dose is burned out. About a hundred cases were treated by Burns and the results are said to have been better than those obtained by the modern methods, and also to have succeeded in cases where salvarsan had previously failed. The inhalations were given daily for 6 or 9 days. The lesions of primary, secondary, and tertiary syphilis healed rapidly, and the Wassermann reaction became negative without further treatment than the original six or nine inhalations. This is the first time we have seen a report of a series of cases treated by fumigation and checked by the Wassermann reaction.

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PULMONARY EMBOLISM AFTER SURGICAL OPERATIONS

Death from pulmonary embolism after a surgical operation is a disaster. A patient apparently recovering well and feeling well is seized without warning and dies within a few minutes. Less often the embolus is small enough to lodge in a branch of the main artery and induces an infarction from which recovery is possible; often, however, a repetition of the embolism is fatal. It has occurred as often as in 1 per cent. of all laparotomies, more frequently after biliary operations, and infrequently after operations on the vermiform appendix. During one year in the Gynaecological Department of the Johns Hopkins Hospital half the deaths were due to this cause. In some 80 per cent. the source of the thrombi appears to be the veins of the leg, and by a process of elimination the conclusion is reached that the origin of such thrombi can only be attributed to a weakness of the heart and consequent feebleness of the circulation.

Septic infection, alterations in the blood or in the walls of the arteries, in the majority of cases are absent, and so cannot be considered essential causes.

The dangerous period is between the sixth and sixteenth day after operation, the danger increasing up to the tenth day and then receding. Meanwhile, in most patients, the force of the heart-beat is improving, so that the determining factor, detaching the embolus from the thrombus, appears to be connected with an increasing force of the circulation, which then carries the embolus through the right side of the heart to the lungs.

It is a general experience that a weak and failing heart may favour thrombosis in the veins of the leg but does not occasion embolism. Even although a thrombosis forms, or there is even also thrombosis in the pulmonary vessels, yet death ensues gradually and not suddenly.

Hampton and Wharton reviewed the cases of pulmonary infarction and embolism which had occurred in the Gynaecological Department of the Johns Hopkins Hospital. A previous report on 40 cases had been made in 1903 by J. G. Clarke, and in 1913 by B. R. Schenck. Thrombosis occurred in 69 cases of operations for uterine myoma, in only one case was there evidence that thrombosis existed prior to the operation. In 17 per cent. there had been preceding anaemia, in 24 per cent. infection of the fallopian tubes, in others pelvic congestion with dilatation of veins and lymphatics. The frequency of thrombosis after operations for uterine myoma may be attributed to coincident changes in the heart-muscle with a consequent weakening of the circulation, but a definite impairment of the heart-muscle under such conditions has not been confirmed, either by clinical examination previous to the operation, or by post-mortem examination of fatal cases.

Between 1890 and 1918, among 21,000 gynaecological operations, perineal and abdominal, there occurred in 205 cases, i. e. in 10 per cent., thrombophlebitis in the femoral veins. 81 per cent. of these followed abdominal operations, 31 per cent. occurred after supravaginal hysterectomy, 11 per cent. after panhysterectomy, 16 per cent. after operations on the uterine adnexa, 10 per cent. after suspensions of the uterus, 5 per cent. after removal of myomas. 8 per cent. were subsequent to perineal operations.

In the cases under the care of the writers, nearly all showed a variable temperature after the operation, preceding the attack of pulmonary embolism. There were in some a persistent pyrexia with swelling and pain in the legs. But some showed no such signs; thrombosis of a large saphena or other vein of the leg may arise without any corresponding pain or swelling. In gynaecological patients thrombophlebitis of pelvic veins is even more important than a similar occurrence in the femoral veins; in 85 per cent. of gynaecological cases the source of the embolus was traced to thrombosis of pelvic veins and in only 15 per cent. to the femoral veins.

Rupp, of Chemnitz, instituted a comparison of the cases of pulmonary embolism after operation with those under medical treatment. Among 13,000 post-mortem examinations during 18 years there were 657 cases (0·5 per cent.) of fatal pulmonary embolism, 290 in males and 367 in females. Of these 56 had happened after operations, 25 within the first week, 13 in the second week, 8 in the third week, 3 in the fourth week, and the remaining 7 within eight weeks.

Among 4,007 abdominal operations excluding hernia there were 30 cases of pulmonary embolism, 18 in aseptic and 12 suppurating cases. Of these, 2,769 operations were on the female genital organs and there were 10 cases of embolism. 168 were operations on the biliary tract with 2 cases the highest percentage, and 1,797 appendix operations with only 1 case.

Of the operations for hernia 1,498 were for reducible and 679 for strangulated hernia; there were 10 cases of embolism, 4 in aseptic and 6 in suppurating cases.

One case occurred among 1,308 operations on the male genito-urinary organs.

12 cases of pulmonary embolism followed 4,758 operations on bones and joints. There were 3 cases among 3,093 operations on the head and neck, 2 following operations for pleural empyema, and 1 for cancer of the larynx.

Thrombi were noted in femoral and iliac veins 26 times on the left and 7 times on the right, 8 times in the uterine plexus, 8 times in the vesicoprostatic plexus, 4 times in the renal and spermatic veins, twice in the haemorrhoidal and once in the axillary. 14 women had evident varicose veins, but no men; 7 women were fat, but this was not noted for men.

By way of comparison Rupp found among 53,000 medical patients, in the course of 18 years, that there had occurred 601 instances of fatal pulmonary embolism, 265 being in men, and 336 in women. 125 of the cases had suffered from forms of pulmonary tuberculosis, 170 from other varieties of disease of the lungs, 248 from heart disease, acute and chronic, 280 from arteriosclerosis, 537 from kidney disease, and embolism terminated 103 cases of carcinoma and sarcoma.

11 of the cases under 10 years of age were all the subjects of exhausting conditions. Thrombi were found in 340 cases situated in the saphena and other tributaries of the inferior vena cava, 264 on the left and 76 on the right. In 99 cases the thrombi occupied the pelvic plexus of veins, in 18 the renal and spermatic. Thrombi were found in the heart in 131 cases, 4 times in the arteries, 7 times in the cranial sinuses, and 13 cases had thrombi in the jugular, subclavian, and innominate veins.

Signs of pulmonary infarction. The occurrence of pulmonary infarction is marked by a sudden onset of pain on breathing, so that a deep breath becomes impossible, but this is distinguishable from the gasping owing to air-hunger attending pulmonary embolism, or that which happens in severe secondary haemorrhage. In at least a third of the cases there is at the same time haemoptysis, the expectoration consisting of bright blood, but this need not appear when the infarctions are small. In cases of extensive infarction the signs approximate to those of pulmonary embolism; there is severe anxiety, fear of approaching death, and the dyspnoea may be attended by shivering and sweating.

Generally the pain is localized below the axilla, below the angle of the scapula, over the lower ribs. Smaller emboli have a predilection for the lower branch of the right pulmonary artery. It is often that it is not until the second day that auscultation discovers signs of pleural friction. Subsequent to this, impairment of resonance and moist râles may be noted.

As distinguished from post-operative bronchitis and broncho-pneumonia, infarctions tend to occur at earlier ages up to 50, bronchitis and broncho-pneumonia in patients over 50. Infarctions are more likely to occur towards the tenth day and end of the second week, by which time any post-operative disturbance of temperature should have subsided. Bronchitis and broncho-pneumonia generally follow the operation within a day or two, there is a gradually increasing cyanosis with rusty sputa and leucocytosis, whereas in the case of infarction there is hardly any or no increase of leucocytes. An old-standing tuberculous lesion, when stirred up by an operation, tends to cause a mucopurulent expectoration containing tubercle bacilli, and any opacity on X-ray examination is likely to be found at the apices and not towards the bases of the lungs.

At the post-mortem the infarction is found to be cone-shaped; its base raises the pleural surface, which is at first smooth, then covered by fibrin.

The infarct is dark purple in colour, its margin is defined by an inflammatory zone, the alveoli of the lung are filled by red corpuscles with only a few leucocytes and are airless. The blood-vessels supplying the affected area are plugged by clot; if there is absorption, the circulation through the affected area is re-established within three weeks. It is only when the emboli are infected that there is a formation of an abscess or gangrene.

There may be a repetition of attacks of infarction or fatal pulmonary embolism may follow an infarction. Of 34 cases of infarction noted by Hampton and Wharton, 5 died, 3 from septic emboli. One had gangrene, one an abscess, and in one an abscess had already formed when there was a final embolism. Another of the five died from pulmonary embolism three weeks after the primary infarction.

Pulmonary embolism. In fatal cases of pulmonary embolism the pulmonary artery and its main branches to the right and left side are found more or less completely blocked. The heart appears to have pumped itself out on the left side and is contracted; the right auricle and ventricle are over-distended by venous engorgement. There are generally no signs of previous disease of the endocardium or of any lesion set up by the passage of the emboli into the pulmonary artery. In the case of sudden death no pathological change may be found in the lung; if the patient is a short while in dying a small degree of general congestion and oedema may be set up; if there is survival for some hours signs of broncho-pneumonia may be found.

In the cases following gynaecological operations, abdominal and pelvic, recorded by Hampton and Wharton, 50 per cent died within 30 minutes, 25 per cent. survived for an hour, 15 per cent. for 24 hours, and 10 per cent. recovered. In some of the examinations the emboli were found to be mobile; emboli may readily become fluid after death, and so none be found in the lungs after removal.

Shaw described three cases which occurred in the same gynaecological service in 1919:

(1) A woman was operated upon for retroposition of the uterus by shortening the round ligaments and removing the appendix. She did well until the twelfth day, when she collapsed and died within 15 minutes. There were thrombi in the pelvic veins and emboli occluded the pulmonary artery and its branches to both lungs.

(2) A woman with high blood-pressure was operated upon for a large umbilical hernia. On the tenth day she developed hesitancy of speech and the left side of the face was drawn; she died the next morning, and there was found pulmonary embolism.

(3) A woman had much fat in the abdominal wall with divarication of the recti. A large mass of fat was removed and the recti drawn together. She got up on the fifteenth day, when she suddenly became cyanosed, had laboured breathing, became unconscious, and died in 15 minutes. A post-mortem examination was refused.

Capelle, in Bonn, noted 15 cases in which a large pulmonary embolism had caused death; in most of the cases a number of small emboli had become rolled together in the heart, and being carried on had blocked the arteries of both lungs. Embolism of one artery was the exception, it was then usually the right, also the detachment of a single embolus was exceptional. In not quite one-half the embolism caused death at once, as if by a stroke of lightning, and death was then entirely mechanical in causation. In the rest there were repeated attacks at short intervals, the signs, increasing with each attack, being pain in the chest, dyspnoea, impairment of resonance, haemorrhagic sputa. Generally the attack was preceded by no warning, the patient, having beforehand recovered from the disturbance of the operation, feeling well and being fully conscious. A prodromal acceleration of pulse and elevation of temperature was exceptional.

Pulmonary infarction and embolism was stated to have occurred in 15 among 10,000 operations, but many cases called post-operative pneumonia are really instances of small pulmonary infarctions. A distinguishing sign is the bright-coloured blood expectorated as compared with the rusty sputa of pneumonia. In only 4 of the 15 were there signs of varicose veins in the lower extremities. 13 presented changes in the back and front of the right lower pulmonary lobes and in only 2 were the signs restricted to the left lung.

12 of the 15 followed laparotomy, none before the fifth day, most between the sixth and fifteenth days, one twenty-four days after the operation.

Trendelenburg had assumed that the diagnosis of pulmonary embolism could be regarded as assured, but Capelle found that in a quarter of the cases diagnosed as such the diagnosis turned out to be erroneous. He proceeded to give instances of erroneous clinical diagnosis, of which three may be quoted as examples.

(1) A fat man, aged 43, suffering from cholelithiasis, underwent cholecystectomy, ether being the anaesthetic used. On the first day afterwards there was slight bronchitis; during the second night, from feeling quite well the patient underwent sudden collapse without loss of consciousness, and without any sign suggesting a peripheral pulmonary infarct. Six hours later there was a further collapse and death within a few minutes. In the lungs were found small peripheral emboli with fresh serous effusion, and a fatty heart especially on the right side.

(2) A cancer of the penis was removed from a man aged 76; on the second day there was slight broncho-pneumonia and the wound suppurated. On the eleventh day the wound was granulating, the temperature normal, expectoration improving, when he suddenly died. There was no pulmonary embolism, only an extremely fatty heart and pulmonary oedema.

(3) A woman, aged 30, had had rheumatic fever and endocarditis; for 14 days there had been signs of thrombophlebitis in the right leg, when she had first one, and then a second attack of what seemed to be pulmonary embolism. She was pale with cyanosis, gasping for breath, the pulse-rate was so quick that it could not be counted, there was dullness over the right base with impairment of breath sounds up to the scapula.

Trendelenburg's operation was begun within 20 minutes of the commencement of the second attack; the heart and respiration stopped whilst the chest was being opened; there was serous fluid in the pericardium and the heart was not beating at all. There was a markedly dilated left ventricle, the left auricle was distended and dark blue, and the distension was continued back into the pulmonary veins. As a result of this distension, the aorta had been twisted forward, so that it was cut into in place of the pulmonary artery hidden under the distended left auricle. Neither the heart nor the respiration could be restarted. There was found on post-mortem examination marked mitral stenosis with congestion of both lungs and blood-stained effusion into the right pleura. No clot was discovered, either at the operation or at the examination after death, in the heart or pulmonary vessels.

Capelle added an account of ten other cases, presenting features similar to the above, in which death had occurred suddenly to patients recovering well after operation, but in whom no thrombosis or embolism could be discovered on post-mortem examination. Of the 15 deaths from pulmonary embolism after operations, 9 died in the first attack, 6 within 5 minutes of the commencement, 3 between 15 and 30 minutes after. All had the main pulmonary artery and its right and left divisions blocked.

In 6 cases there were slighter attacks preceding the fatal one. One of the cases was operated upon for the removal of the embolus, the operation commencing just as the death struggle ended. Four cases died within 2–7 days after the commencement of the first attack; in 2 the attacks were diagnosed as due to broncho-pneumonia, in 2 the attacks were deemed faintings; 2 cases appeared to recover spontaneously from the first attack, diagnosed as pulmonary embolism, and one of them died three months after a previous attack.

As to Trendelenburg's operation for the removal of the pulmonary embolus, there are many objections to the dictum that after one definitely diagnosed attack of pulmonary embolism a patient should be submitted to the operation immediately upon what appears to be a commencement of a second attack. There is then not only the question of the correctness of the diagnosis but the further difficulty that cardiac lesions, engorgement, pericardial effusion, &c., may be encountered.

Granted an attempt at the operation on a dying patient, as soon as the pulmonary artery is exposed, the first step should be to get rid of the venous engorgement of the right side of the heart. The assistant's hand should be passed behind the heart so that with his fingers and thumb he can compress the junction of the venae cavae with the right auricle. Then the commencement of the pulmonary artery is incised and the blood filling the right side of the heart squeezed out. Next comes the removal of the clot from the pulmonary artery beyond the incision. If a pleural exudation has collected on the right side the heart may have been pushed over, when the aorta is likely to be twisted forward and may then be mistaken for the pulmonary artery.

As to the prevention of pulmonary embolism recent observations do not afford assistance. If it be the case that a weakened heart favours thrombosis, but that it is a heart improving in force which determines the embolism, then proposals to administer cardiac stimulants or to get patients up early are of very doubtful expediency. The proposal to ligature the termination of the internal saphena when thrombosis occurs in its tributaries may be objected to as entailing possible dangers following that operation.

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W. G. S.

GANGLIONEUROMATA

Ganglioneuromata are tumours which contain fully-formed nerve ganglion cells, corresponding in appearance with the cells of the sympathetic nerve ganglia. They are usually benign, at any rate for a long while, but tend finally to develop malignant characters. Those in particular which arise in the medulla of the suprarenal capsule are often, although not necessarily, very malignant from the first and are then distinguished as neuroblastomata. It is clear that all ganglioneuromata arise from 'rests' of the embryonic nerve-tissue from which develop the sympathetic ganglia. Neurocytes in these 'rests' develop in the benign tumours into ganglion cells, with their capsules and ring of small round cells, also into neuroglia, and medullated as well as non-medullated nerve-fibres form the stroma of the tumour. In the tumours which have become malignant, instead of the ganglion cells there are seen irregular groups of embryonic neurocytes with non-medullated nerve-fibres. The neuroblastomata have the course and structure of small round-celled and oval-celled sarcomata in the parts which are growing the most rapidly.

The first instance of a ganglioneuroma was noted by Günsberg in 1845. A tumour, the size of a pigeon's egg occupied the position of the Gasserian ganglion, and presented an increase of ganglion cells which he estimated to amount to ten times the number contained in the normal ganglion.

In 1870 Loretz found a tumour the size of an egg in the thorax, to the left side of the spine, at the level of the 2nd and 3rd dorsal vertebrae. It had infiltrated superficially the vertebrae, and was spreading through an intervertebral foramen into the spinal canal. It contained ganglion cells, singly or in nests, with non-medullated fibres for stroma, also a few medullated fibres, and it had grown from a sympathetic ganglion of the lateral chain.

In a similar tumour noted by Friedrich, removed *post mortem* from a woman aged 73. It was the size of a goose's egg and had been fixed to the right side of the vertebral column opposite to the 6th–8th vertebrae, behind the pleura. It had not invaded the vertebral column, or involved the spinal canal. The sympathetic lateral chain was connected with each pole, and from its side next the vertebrae the great splanchnic nerve passed downward. The tumour was a ganglioneuroma with relatively few ganglion cells, and a mass of non-medullated nerves, exhibiting axis cylinders, sheaths of Schwann, and spindle-shaped nuclei. This case showed that a tumour may remain benign until old age.

Suprarenal ganglioneuromata. Very malignant tumours arising in the suprarenal capsule have been described as small round-celled sarcomata of young children. But as distinguished from undifferentiated small round-celled sarcomata, some of the cells are found arranged in groups resembling the appearance noted in the developing sympathetic nervous system and medulla of the suprarenal gland, besides, a network in the tumour stains like neuroglia.

The medullary portion of the suprarenal gland is dark in colour owing to venous sinuses containing blood; it stains a yellowish-brown with chromic acid owing to the so-called chromaffin action of the chromic acid upon secreting cells. In addition, there are cells derived from the blastoma forming sympathetic ganglia. In elasmobranch fishes the medulla of the suprarenals is represented by paired bodies in close relation with the ganglia of the sympathetic nervous system. In the case of the more benign suprarenal ganglioneuromata the origin of the tumour from the medulla of the gland can be demonstrated.

Hook found *post mortem*, in a boy who had died of acute infective osteomyelitis of the tibia, a tumour of the right adrenal, the size of a walnut. It lay under the capsule of the kidney, in the substance of the adrenal and measured 4·5 × 1 cm. in diameter. It was soft and whitish on secretion; microscopically, it proved to be a ganglioneuroma of a benign character.

In the case of a similar tumour described by Hedinger cystic degeneration had occurred, but the tumour had continued benign. A woman, aged 34, had died after aborting at 4½ months. The tumour of the left suprarenal, measuring 10 cm. in diameter, was encapsuled, with the capsule adherent to the diaphragm and tail of the pancreas; it lay entirely behind the peritoneum. There was a cavity in the tumour 8 cm. in diameter, containing a pale yellow fluid and lumps of brownish fat. The wall of the cyst, 2–3 cm. thick, had the structure of a benign ganglioneuroma; the suprarenal cortex had almost entirely disappeared. Wassmund found in the medulla of the right suprarenal of a man, aged 26, a tumour the size of a walnut, composed of sympathetic ganglion cells and nerve-fibres, medullated and non-medullated, which were tending to infiltrate the cortex of the gland.

Wahl examined *post mortem* a girl, aged 2½, who had died after suffering for several months from severe abdominal disturbance with anaemia. A neuroblastoma had arisen in a suprarenal and had extended to retroperitoneal and retropleural lymphatic glands. In the position of the left adrenal below the spleen was a tumour adherent to the kidney, into which the growth had penetrated as far as the pelvis. Remains of the normal adrenal gland were found embedded within the tumour. Its cortex and part of its medulla were normal in appearance; the tumours had grown out from part of the medulla. Extensions to the lymphatic glands surrounded the aorta, vena cava, and portal vein in the hepatic fissure. The liver was yellowish-brown and studded with round opaque nodules 2–2·5 cm. in diameter; the right kidney also presented a few metastases, but the right adrenal was normal. The structure of the primary tumour was that of a ganglioneuroma; the structure of the metastases resembled embryonic nerve-tissue showing embryonic sympathetic ganglion cells, non-medullated fibres, and neuroglia, with some tendency to cystic degeneration. Also in places there was soft, very vascular, undifferentiated sarcomatous tissue tending to haemorrhagic degeneration.

A neuroblastoma growing in a suprarenal may give rise to a single distant metastasis to which, in the first instance, attention may be solely directed. Thus Symmers described a tumour in the scapular region which was recognized as to its origin by finding it composed of embryonic sympathetic ganglion cells, arranged singly or in groups, also cells resembling neurocytes with little protoplasm and highly staining nuclei, situated in a tangled mass of fibres which stained like embryonic neuroglia. The tumour had recurred after its removal.

On the other hand, a suprarenal new growth may first show itself by multiple metastases. In Gunby's case these were limited to lymphatic glands and bones, whilst none were found in the viscera. A boy, aged 13, had had for six months increasing weakness, chlorosis, failing vision, exophthalmos, and lumps fixed to the skull. Optic neuritis was discovered; for a month before death there were pains in the knees and hips, also tenderness over the sternum and ribs, and the cervical glands became enlarged on both sides. There was, however. little headache and no vomiting.

In correspondence with the tumours on the skull, the X-rays showed a diffuse porosity; there was a large smooth mass, fixed in the hypochondrium below the liver. After death it was found that a neuroblastoma had arisen in the left suprarenal capsule and had infiltrated the neighbouring retroperitoneal glands. The skull was honeycombed by a number of tumours which had pressed the dura mater inward and also protruded under the scalp. The region of the optic nerves had become involved and the sphenoidal fissure blocked. The sternum and ribs were similarly infiltrated to a less advanced stage. The tumours were mainly cellular, the amount of stroma being small, but varying. The cells closely resembled round and oval leucocytes with deeply staining nuclei, but in places there were clumps of cells resembling neurocytes.

In a case described by Knauss in 1898—another under Guervain was recorded by Geymüller—multiple metastases appeared in the subcutaneous tissue without at the time affecting the patient's general health, the case clinically resembling one of Recklinghausen's neurofibromatosis.

Knauss found in a girl, aged 9, whose general health was not impaired, numerous tumours under the skin all over the body. They had appeared first at the age of 3 years. A number were removed and found to have the structure of ganglioneuromata. The incisions healed by first intention.

As to the removal of suprarenal ganglioneuromata, the smaller and benign tumours appear to have been found only *post mortem*. The malignant neuroblastomata, when discovered, were inoperable. Brieger operated on a girl, aged 8, for a tumour diagnosed as renal, on the left side. Previous to the operation, the excretion of the left kidney was found deficient, as it turned out, owing to compression of its pelvis by the tumour. An X-ray examination, after air had been let into the peritoneal cavity, disclosed a shadow in front of the tumour, which was taken to represent the spleen, although really the kidney. At the operation the tumour was distinct from the kidney, which it had pushed forward, compressing the pelvis. It was connected with the suprarenal capsule by a strand. The child died as the operation was being completed. The tumour showed cells resembling ganglion cells and irregularly arranged nerve-fibres, the periphery of the tumours being vascular.

Mesenteric ganglioneuromata. Ganglioneuromata grow in the prevertebral sympathetic plexuses and are found as benign encapsuled tumours situated between the layers of the mesentery or behind the peritoneum. In 1899 Cripps and Williamson found in a woman, aged 21, a tumour adherent to the front of the sacrum, behind the peritoneum. It was detached partly by the knife, partly by the fingers, a large nerve being noted running through it. The tumour appeared like a soft myxoma, and was found to be composed of sympathetic ganglion cells and non-medullated nerve-fibres.

MacNaughton Jones removed a tumour from the mesentery which was described by H. M. Turnbull to be partly a benign ganglioneuroma, partly a malignant neuroblastoma. The girl had been noted, at the age of 5, to have an abdominal tumour, which by the age of 10 had reached the size of a large orange. It lay below and to the left of the umbilicus, covered by omentum and small intestines, between the layers of the mesentery, from which it was shelled out, after a pedicle from which there was venous haemorrhage had been ligatured. The tumour measured 15 × 11 × 10 cm., and seemed to be passing from a benign to a malignant stage.

Peterson's case, similar to the above so far as the position of the tumour, arose in a boy aged 9, and was easily enucleated. It measured 6·5 × 4 cm. The periphery of the tumour was fibrous in character; the centre, soft and reddish, showed ganglion cells and medullated nerve-fibres. The fibrous periphery contained strands of unstriped muscle, evidently derived from those fibres which are found in the mesentery of children.

In Bland-Sutton's case an attempt had been made to remove a tumour when the boy was aged 4, but the operation had been abandoned. When the boy had reached the age of 10 Bland-Sutton removed a tumour 15 × 10 cm. in diameter from between the layers of the mesentery. The tumour had a firm yellowish periphery and a soft centre; it was composed of ganglion cells and medullated nerve-fibres.

Cervical ganglioneuroma. In 1900 Burghard excised a tumour of the superior cervical ganglion of the sympathetic; in structure it proved to be a fibromyxoganglioma.

Geymüller noted, in a boy aged 5, a tumour the size of an egg, situated between the mastoid process and the upper cervical vertebrae. It was easily shelled out and found to be a ganglioneuroma with an excess of non-medullated nerve-fibres; it had evidently developed from the superior cervical ganglion. Guervain had observed a tumour in this position for a long while before multiple subcutaneous tumours appeared.

Sommerfelt observed what was supposed to be an enlarged submaxillary lymphatic gland in a woman aged 36. In the course of six years it grew to the size of a goose's egg; when removed it was definitely circumscribed except for four fine strands suggestive of nerve-fibres. The results of the examination of the tumour were depicted in 25 coloured drawings by Fräulein Morah.

The surface of the tumour was semi-translucent, in colour greyish-white, with a yellowish tinge, which under the microscope appeared as a fibrous stroma, with blood-vessels and collections of lymphatic gland tissue. Scattered amongst the fibrous and lymphatic gland tissue were ganglion cells, medullated and non-medullated nerves; some nerve-fibres could be traced into ganglion cells. There were also peculiar round cells which could be differentiated by staining, and which contained a granular protoplasm and pigment. Various stages could be recognized from round cells representing the neurocytes up to fully-formed ganglion cells surrounded by capsules with small cells. The tumour was presumed to have arisen in the submaxillary ganglion.

Ganglioneuromata in the central nervous system. Ganglioneuromata have been met with in quite different parts of the central nervous system. They have been generally benign in character, so circumscribed as to admit of removal, and composed of fully-developed ganglion cells and neuroglia. Schmincke found in the right temporo-sphenoidal lobe of a man aged 17, a tumour the size of a large walnut, which shelled out readily. He had suffered from epilepsy since the age of 8. The tumour consisted of loose fibrous tissue with nuclei like connective tissue, also of fibres staining like neuroglia, of fully-developed ganglion cells, apolar and bipolar, of embryonic ganglion cells and of non-medullated nerve-fibres. There were no completely medullated nerve-fibres.

Pick and Bielschowsky found in the medulla of a woman, aged 24, a ganglioneuroma, similar in structure to the foregoing. The only symptom during life had been hiccough.

Robertson described such a tumour in the floor of the 3rd ventricle which had involved the optic chiasma.

In Berblinger's case a girl, aged 17, had suffered from the general signs of cerebral tumour, severe headache, optic neuritis, and epileptiform fits. The tumour was situated in the septum pellucidum.

In Olivecrona's first case a man, aged 39, was suddenly seized with pain and rigidity in the neck; loss of consciousness followed, and death within a week. The tumour was situated in the right temporal lobe and was 7 × 6 cm. in diameter. The tumour differed from others belonging to the central nervous system in that it contained medullated nerve-fibres; all the ganglion cells were fully developed. His second case arose in the under-part of the right frontal lobe and spread across the middle line. The patient had suffered from spastic rigidity of the left arm. The tumour contained ganglion cells of the embryonic type, with non-medullated nerve-fibres and neuroglia.

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W. G. S.

THE CLINICAL PICTURE OF COMPLETE TRANSVERSE DIVISION OF THE SPINAL CORD

Hitherto there has been no complete review embodying the experience of the past seven years on the clinical picture of transection of the spinal cord. The war has greatly extended our knowledge of this subject, and has enabled us to appreciate the true value and significance of the pioneer contributions of Bastian, Collier, and others in the period preceding the war. The present review is an attempt to summarize recent additions to knowledge and to correlate these with earlier work.

In a paper read before the Medico-Chirurgical Society in 1890, Bastian made his well-known generalization that muscular flaccidity and absence of tendon reflexes in the lower limbs is the permanent result of total transverse lesions of the spinal cord in the lower cervical and upper dorsal regions. The symptomatology he described is as follows : Complete atonic paralysis of the muscles of the lower extremities and abdominal wall ; loss of sensibility below the level corresponding to the spinal lesion ; only slight wasting of the paralysed muscles even after a long period ; abolition of abdominal and cremasteric reflexes and knee- and ankle-jerks, the only reflex response to remain being an occasional slight movement of the toes when the sole of the foot is strongly tickled ; dry skin ; retention of urine for the first ten to fourteen days followed by periodic reflex evacuation of the bladder which is never complete; retention of faeces. The toe-response in a patient examined by Collier, and three patients examined by Walshe, was 'extensor' in form, and the latter found that it was accompanied by slight flexion at hip and knee and dorsi-flexion of the foot.

Bastian's doctrine was accepted on the whole in this country and abroad up to the time of the recent war, though it was assailed in several important contributions to the literature which showed that, at all events, there were exceptions to the rule. Most of the controversy ranged round the presence or absence of the tendon reflexes. In the majority of the reported cases they were absent; but Collier, Lewandowsky and Neuhof were able to show that prolonged faradization of the muscles might allow the knee- and ankle-jerks to be obtained even a few days after the onset of paralysis.

But Bastian and his followers, in arriving at the conclusion that transection of the spinal cord in man permanently suppressed the reflex function of the isolated portion, did not appreciate the importance of two considerations: (1) that from early death of the patient the period of observation was short, and (2) that toxaemia from urinary or pulmonary complications or septic bed-sores may be the cause of abolition of function by leading to structural alterations in the reflex arcs.

Investigations carried out in the recent war on the results of complete division of the spinal cord by high velocity projectiles have conclusively proved the probability of recovery of reflex activity in the paralysed parts if life is prolonged even for a few weeks and serious complications are absent.

In order to appreciate the significance of the phenomena observed and establish rational methods in nursing and general treatment, it is essential to recognize the difference between early and late effects of spinal transection. The clinical course may be divided into three stages: (1) reflex depression or spinal shock, (2) reflex excitability, and (3) gradual failure of reflex functions. The third stage develops only if severe toxic infections appear late and lead to the death of the patient.

Stage of reflex depression or spinal shock. When the spinal cord is suddenly divided in the lumbar thoracic or lower cervical regions, there is immediate complete and permanent paralysis and loss of sensibility in the parts innervated by the portion of the cord caudal to the lesion. The nervous system above the site of injury is unaffected by the lesion and consciousness is unclouded. The patient feels as if he has been 'cut in two', and, when the trunk and four limbs are paralysed from division of the cord in the lower cervical region, he may imagine that, except for his head and neck, his whole body has been blown away. As a rule, he is remarkably free from pain.

Muscle tonus: According to Guillain and Barré, Roussy and Lhermitte, muscular tonus is often at first neither diminished nor increased, the paralysed muscles retaining their normal contour and consistence. Within a few hours or days, however, flaccidity definitely develops and persists until reflex activity returns. The limbs lie in any position in which they are passively placed; they are flail-like, and excessive displacement appears to be prevented mainly by the anatomical configuration of the joints.

Reflexes. The depression of reflex activity is always profound, and, as regards the abdominal wall and lower extremities, may be complete. Not infrequently, however, in response to nocuous stimulation of the skin, certain reactions can be evoked, especially those which depend upon reflex arcs of the caudal segments of the cord. Thus the bulbo-cavernosus, anal, and plantar reflexes are often present, and may be evoked very soon after the injury.

Attention has been especially directed to the forms of response excited by scratching the sole of the foot. Guillain and Barré, in fifteen out of sixteen cases of recent injury, obtained downward movement of the toes as the only response to plantar stimulation. This movement differed from the normal 'flexor' response in being delayed and slow both in development and subsidence. Usually it first appeared from twelve to twenty-four hours after the injury, but on one occasion it was obtained less than an hour after the spinal transection. In one case it was present as a crossed response only; that is to say, on scratching the sole of one foot, the downward movement was confined to the toes of the other foot.

Other observers (Déjerine and Mouzon, Holmes, Roussy and Lhermitte, Riddoch) have described this reaction, and it is probably the most common form of toe-response to be obtained in the early days of the illness. However, it is soon accompanied by contractions of the flexors of the hip and knee and dorsi-flexors of the foot, and, at a later stage, it is replaced by upward movement of the toes.

Sometimes downward movement of the toes fails to appear as the earliest response to plantar stimulation, and from the first the toes are displaced upwards when the sole is scratched (F. Rose, Lévy, Déjerine and Mouzon, Riddoch). Roussy and Lhermitte mention a case in which upward movement of the toes was evoked less than an hour after the injury. When of this form the reaction from its earliest appearance includes contraction of the hamstrings and other flexor muscles of the limbs.

With high lesions the cremasteric reflexes can often be excited by appropriate stimulation within a few days from the date of the injury, and more rarely about the same time reflex contraction of the abdominal muscles on the side of the stimulation can be obtained. Riddoch records an example of complete spinal transection at the level of the fourth thoracic segment where abdominal reflexes were readily excited seven days after the injury. The extent of the reaction varied with the strength of the stimulus. Thus on gently scratching the skin over the external oblique, a localized contraction of the muscle was evoked which followed the course of the muscular fibres. A firmer scratch applied over a larger area of skin elicited strong contraction of the rectus and lateral abdominal muscles on the same side. The response in either case was strictly unilateral but could be evoked on each side.

With regard to the knee- and ankle-jerks, the rule, with few if any exceptions, is that for the first fortnight after the injury the extensor tendon-jerks of the lower extremities are absent irrespective of the situation of the spinal lesion above the lumbar enlargement. On the other hand, contraction of the hamstring muscles in response to tapping the appropriate tendons may be obtained quite early, and Guillain and Barré and Lhermitte have observed this reaction to follow percussion of the patellar tendon.

Vasomotor, pilomotor, sudorific, and nutritional changes. Vasomotor reactions are preserved but are sluggish, so that the paralysed parts of the body tend to lose heat with unusual rapidity. Dilatation of the cutaneous blood-vessels follows friction of the skin, but the reaction is delayed and tends to persist unduly after removal of the stimulus. The ankles and feet rapidly swell if the limbs are allowed to hang down, and the nutrition of the tissues is lowered so that the skin breaks down readily under continued pressure. The process of healing is much delayed.

According to Roussy and Lhermitte, pinching the skin may evoke erection of hairs, but even in the presence of fever there is an entire absence of sweating from the skin covering the paralysed regions.

Bladder, rectal, and sexual functions. Irrespective of the situation of the spinal lesion there is retention of urine and faeces. The experimental observations of Head and Riddoch show that although the stage of retention of urine usually lasts for about three weeks, the reflex activity of the detrusor often begins to recover within a week of the spinal injury.

Priapism, a result of vasomotor disturbance, is occasionally observed as a temporary phenomenon following the injury to the spinal cord, but there is no true erection of the penis or seminal emission.

Stage of reflex excitability. In from three to four weeks after the date of the injury (Roussy and Lhermitte, Riddoch) the depression from spinal shock begins to pass off, and for three or four months in uncomplicated cases, reflex activity progressively increases. The paralysed parts respond more and more readily to stimulation and reflex movements, usually violent, dominate the clinical picture. All authorities are agreed that by far the most common reflex movements of the trunk and lower extremities are flexor.

Reflex flexion of the lower limbs and trunk. Pricking and scratching the sole of the foot evokes withdrawal of the lower limb, the movement consisting of flexion at the hip and knee, dorsi-flexion of the foot, and upward movement of the toes. This is the well-known flexion reflex which Sherrington originally described in decerebrate and spinal animals. In 1914, Walshe investigated the reaction in spastic states in man following lesions of the pyramidal tract, and showed that the so-called extensor plantar response of Babinski is part of the general withdrawal or flexor movement of the limb. Examination of the reflex in spinal man led Riddoch to the same conclusion.

At the beginning of the stage of reflex activity, the flexion reflex can be excited from the sole of the foot only and especially from its outer part; but soon the receptive field extends from this focus, and usually in time comes to comprise the whole of the lower limb (Riddoch, Lhermitte, Roussy and Lhermitte). Throughout the clinical course the most effective forms of stimulation are those which are potentially harmful and painful. Thus pricking or scratching the skin or pinching the deep tissues of the lower extremity readily excite the reflex. The excitability of the reflex arcs tends to become progressively greater, until within three or four months of the injury violent flexor spasms may follow slight increase in the tension of the flexor muscles, friction of the bed-clothes on the skin, gentle 'tickling' of the sole of the foot or inner aspect of the thigh, or even exposure of the limb to a current of air (Riddoch, Claude and Lhermitte). Careful investigation of the so-called spontaneous or automatic movement of the lower limbs, which from their violence and frequency are so distressing to the patient, shows that they are the result of some form of peripheral stimulation. Hence, the first principle in treatment is to protect the paralysed parts from stimuli which are capable of evoking spasmodic movements of the limbs (Riddoch).

When the flexion reflex first appears, the reaction may consist merely of contraction of the flexor muscles of the large joints and upward displacement of the toes. This forms the minimal response to appropriate stimulation. In the full development of reflex activity, however, although the strength of the reaction can be often graded to some extent by varying the strength of the stimulus, this is by no means constant. At any time the gentlest effective stimulus may evoke the maximum response. One of the most important factors upon which irregularity of strength of response to strength of stimulus depends is the state of the limb prior to the application of the experimental stimulus (Riddoch). If before stimulation the limb has been the subject of repeated violent flexor spasms, a minimal effective stimulus will tend to evoke a maximum reaction. On the other hand, a response graded to the intensity of the stimulus is more apt to be obtained when the limb had previously been inactive.

A characteristic feature of the flexion reflex response in spinal man is that the locality of the stimulus has comparatively little effect in varying the form of reaction evoked. Thus there are usually only minor differences between the reactions evoked from the sole and from the groin (Riddoch).

When the reflex arcs are highly excitable the flexor movement develops explosively and the attitude of flexion tends to be maintained for some time after the brief stimulus has been removed. The subsequent incomplete extension of the limb is often due only to relaxation of the flexors and the action of gravity. Less frequently extension is brought about by active contraction of the extensors.

The response may be confined to the stimulated lower limb, but even with a mild stimulus a much more extensive reaction may be obtained. In a number of cases contraction of the extensor muscles of the crossed lower limb with downward movement of the foot and toes accompanies the flexor movement evoked in the stimulated lower extremity (Lhermitte, Riddoch). Extension of the crossed lower limb may be of short duration and replaced quickly by flexion. The complete response to nocuous stimulation, however, which is found most commonly has been described by Head and Riddoch as a mass-reflex. It consists of bilateral flexion of the lower limbs and trunk, profuse sweating, and evacuation of urine and faeces. The reaction follows stimulation of the lower limbs or the paralysed part of the trunk as well as of the bladder and rectum. Bilateral flexor spasms and hyperidrosis accompany reflex micturition or defaecation, and are very liable to be provoked by irritating bed-sores, intestinal disorders, cystitis, inflammation of the glans or prepuce, or obstruction of the urinary outflow.

Reflex extension of the lower limbs and trunk. In the absence of toxaemia from septic complications evidence of excitability of the extensor reflex arcs can usually be obtained a few weeks after the date of spinal transection. With lesion above the lumbar enlargement the knee-jerks return, as a rule, about three weeks after the injury, followed later by the ankle-jerks (Riddoch, Marinesco, Lhermitte, &c.). Ankle clonus, which is usually poorly sustained, can be evoked in many cases. Although the extensor tendon-jerks become brisk and easy to excite they differ from the reactions in hemiplegia and spastic paraplegia in extension in the quick falling away of the contraction (Riddoch, vide *Medical Science*, 1920, **2**, 346). The explanation of the difference is that extensor tonus is much diminished after spinal transection whereas it is increased when the lesion of the descending motor pathway is confined solely or mainly to the corticospinal tracts.

Tendon-jerks, however, bring into action muscles which play on one joint only. Reflex reactions which involve all the extensor muscles of the limb are much less frequent than reflex flexion, and when present are usually secondary to it. Thus active extension of the limb has been observed to follow reflex flexion, and it may occur in the opposite lower extremity in association with a flexion reflex (Lhermitte, Roussy and Lhermitte, Claude and Lhermitte, Riddoch).

Primary extension reflex reactions are very rarely evoked directly by stimulation. According to Lhermitte, extensor-adductor spasms are sometimes observed, and Schaller and Cadwalader in two old-standing cases were successful in evoking contraction of the extensor cruris muscles by passive movements of the knee. In Schaller's patient the reaction was obtained eighteen months, and in Cadwalader's nineteen years, after the injury.

Primary extensor reactions appeared in one of nine cases investigated over long periods by the writer. This patient was wounded at the level of the fourth thoracic segment, and showed the usual preponderating flexor movements and spasticity for the first ten months after the injury. Then, simultaneously with diminution of the spasticity and flexor spasms, primary extension reflexes appeared. For example, sudden dorsi-flexion of the foot evoked extension at hip and knee, and downward movement of the foot and toes; and a similar response, usually bilateral, followed nocuous stimulation of the thigh or perineum or movement of the prepuce over the glans penis. The brief symmetrical bilateral response evoked from the penis was accompanied by retraction of the anterior abdominal wall. Lhermitte has obtained extensor movements of the stimulated lower limb by stimulation of the posterior aspect of the thigh, but the crossed response in this case was flexion.

Thus, although the extensor tendon-jerks recover almost invariably in uncomplicated cases of spinal transection above the lumbar enlargement, they appear considerably later than the flexor (hamstring) tendon-jerks and usually fail to show tonic prolongation of contraction. Further, extension of the lower limb as a whole is a much less frequent reflex phenomenon than flexion. When present as a rule it either accompanies reflex flexion as a crossed reaction or follows upon it in the same limb. In a small number of cases, usually of long standing, primary extension of one or both limbs can be evoked by suddenly increasing the tension of extensor muscles or by stimulation of the thigh, perineum, or external genitalia.

In general, spinal transection in man has the effect of heightening the activity of flexor and lowering the activity of extensor reflex arcs.

Rhythmic movements. Rhythmic alternating movements of flexion followed by extension of the one or both lower limbs are described by Lhermitte. In the experience of the writer they are rare, especially as bilateral reactions; they were present in one out of nine cases, and in this instance they appeared ten months after the date of injury. The movements were confined to the feet and toes and upward movement of one foot was accompanied by downward movement of the other. When they were evoked by passive dorsi-flexion of one foot, downward movement of the foot and toes on the side of stimulation and upward movement on the opposite side formed the opening phase; whereas the opposite primary movement was obtained by scratching the skin of the sole. However evoked the rhythmic alternating movements of the feet, reminiscent of the stepping movements of the spinal dog or cat (Sherrington), often continued at a regular slow rate for a short time.

Roussy and Lhermitte describe rhythmical contractions of the abdominal muscles evoked by stimulation or appearing to arise spontaneously. The rhythm did not correspond with that of the pulse or respiration.

Muscular tonus. Under favourable conditions tonus begins to return in the flexor muscles of the lower extremities about the time of appearance of the flexion reflex and involuntary flexor movements. Usually flexor tonus and reflex excitability increase together, and, unless measures are taken to prevent them, flexor contractures of the lower limbs may develop.

Throughout the clinical course the tonicity of the extensors remains below that of the flexors although the knee- and ankle-jerks, as a rule, return, and spasmodic extensor movements of the lower limbs may occur (Riddoch, Marinesco, Cadwalader). Permanent extensor rigidity has not been described. After the lower extremities have been passively extended they often return to a position of flexion at hip and knee. Predominant flexor spasticity was the condition observed by Cadwalader in a case of complete spinal transection in the lower thoracic region nineteen years after the injury; and extensor hypertonus could be evoked as a transient phenomenon only by passive movements of the knee.

Electrical excitability of the paralysed muscles and their nerves. The response to the faradic and galvanic currents may be normal (Lhermitte) or diminished (Marie and Foix, Lhermitte). Rennie noted in one patient four and a half years after transection in the upper thoracic region, that electrical excitability of the paralysed muscles was greatest in the morning, and tended to be diminished in the evening especially when spasmodic movements of the limbs had been frequent.

Bladder, rectal, and sexual functions. The period of retention of urine is followed, after about three weeks, by reflex micturition (Head and Riddoch). At first evacuation of urine is irregular and incomplete; but within a few weeks, if the general health of the patient is good, the bladder is reflexly emptied at fairly regular intervals which vary from one-half to two hours in different cases. The length of the interval between the reflex acts depends upon the amount of urine that forms the appropriate tension stimulus to excite the vesical reflex arcs. The effective fluid content ranges from about 300 c.cm. to 700 c.cm. in different cases; but Head and Riddoch have shown that in each case the quantity of contained fluid with which the bladder 'fires off' can be greatly diminished by extravesical stimulation. Thus by exciting reflex defaecation or a flexor spasm of the lower limb or by asking the patient to breath deeply, the contents of the bladder may be voided when they amount to less than half the quantity with which the bladder usually reacts. Conversely, reflex micturition frequently excites a flexor spasm of the lower limbs and trunk, reflex defaecation, and excessive sweating.

Facilitation of reflex micturition by evoking flexor movements of the lower limbs has also been described by Roussy and Lhermitte.

The reflex arcs of the rectum recover about the same time as those of the bladder, and if the rectal contents are kept soft by the administration of laxatives reflex defaecation periodically takes place.

Penile erections with seminal emissions may occur spontaneously or be evoked by appropriate stimuli, and are not infrequently accompanied by reflex movement of the lower limbs and trunk. Reflex evacuation of urine inhibits erection of the penis (Riddoch).

Vasomotor, pilomotor, sudorific, and nutritional changes. According to Roussy and Lhermitte oedema of the lower limbs, circulatory disorders, and bed-sores are most prominent during the stage of reflex activity. This has not been the experience of the writer, who found that in healthy patients these troubles tended to disappear.

Mention has already been made of excessive sweating as a frequent symptom of this stage, even in the absence of fever, and of its common association with involuntary movements of the lower limbs and reflex micturition and defaecation. The area of hyperidrosis covers the paralysed parts of the body, but its upper limit does not necessarily correspond to that of anaesthesia (Head and Riddoch, Thomas). The experiments of Head and Riddoch have demonstrated the reflex origin of this sweating through the connexions of the sympathetic with the spinal cord (thoracico-lumbar outflow). These observers have also related the upper limit of the area of hyperidrosis with the level of the spinal lesion. Thomas has shown that the pilomotor reflexes recover before sweating appears on the skin of paralysed parts.

Stage of gradual failure of reflex functions. The case of total division of the cord of nineteen years' duration recently recorded by Cadwalader shows that the stage of reflex activity may last for a long time provided the general health of the patient remains good. Not uncommonly patients live for several years and are able to go about in self-propelled chairs. But their resistance to infections is low, and if toxaemia develops and persists they tend to deteriorate rapidly. Poisoning of the isolated portion of the cord is expressed in gradual failure of its reflex functions. Reflex activity diminishes, the extensor tendon-jerks disappearing before the flexion reflex; the muscles waste and lose their tone, and retention of urine and faeces may return before death supervenes.

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G. R.

ABSTRACTS

NEUROLOGY

Lhermitte, J. The anatomical and clinical syndromes of the corpus striatum. *Neurol. Bull.*, 1921, **3**, 163.

Lhermitte gives an interesting précis of the abundant literature which has been published on the symptomatology and pathology of the corpus striatum within the past few years. As such it is not readily capable of abstraction, but the paper having been published in two relatively inaccessible journals, and the subject having as yet received no similar treatment in this country, a short account of Lhermitte's review may be of value. Several of the papers quoted have already been reviewed in *Medical Science*, and the references are here given.

I. Lhermitte deals first with **the gross and fine anatomy of the corpus striatum** and with its fibre connexions. The caudate nucleus and putamen are grouped together as the striatum, while the two inner segments of the lenticular nucleus are spoken of as the pallidum. The term corpus striatum is employed to designate both parts of the structure together. The striatum contains nerve-cells of Golgi Types I and II. The pallidum contains Type I cells only. The latter contain both Nissl and lipochrome granules. The small Type II cells show neither. Fine fibres pass from both parts of the striatum to the pallidum, but no projection fibres leave the corpus striatum from this part of the nucleus. The axones of the large cells of the pallidum, on the other hand, form an important projection tract, the ansa lenticularis, which sends fibres to the thalamus, nucleus of Luys, red nucleus, substantia nigra, and to the region of the cerebral peduncles. Afferent fibres to the corpus striatum come from the thalamus alone. There are no fibre connexions with the cerebral cortex. It appears, therefore, that the corpus striatum, completely independent of the cerebral cortex, forms an anatomically autonomous system, whose afferent fibres arise in the thalamus, and whose efferent fibres arising almost exclusively in the pallidum pass to the thalamus and to masses of grey matter in the subthalamic region.

II. Lhermitte dismisses **the experimental physiology of the corpus striatum** very summarily, because it has been almost uniformly negative in its results. This is undoubtedly true, but whether we are justified in believing that these negative results have no significance is another matter.

III. **Anatomo-clinical observations** are very numerous and are the source of such information as we possess of the activities of the corpus striatum. On the basis of anatomical and histological differences it is assumed that the striatum and the pallidum are different in function. There is some clinical support for this view, and the attempt has been made to elaborate syndromes of the corpus striatum as a whole, and of the striatum and pallidum singly. Lhermitte gives the following syndromes:

A. **Syndromes of the corpus striatum (striatum + pallidum).**

i. *Progressive lenticular degeneration (Wilson's disease).* The cardinal features of this are diffuse muscular rigidity leading to a characteristic attitude and facies and ultimately to contractures, and to dysarthria, aphonia, and dysphagia. Spasmodic laughter and weeping occur and also involuntary movements of the tremor and athetosis variety. Peculiar to the disease are lesions in the viscera, hepatic cirrhosis, and sclerotic changes in spleen and pancreas. The disease develops in childhood and is often familial. The nervous lesion is atrophy and sometimes extensive cavity formation in both portions of the corpus striatum. The ansa lenticularis is markedly degenerated.

ii. *Pseudosclerosis (Westphal-Strümpell).* This is now regarded in Germany as identical clinically and pathologically with progressive lenticular degeneration (*Medical Science,* 1919, **1**, 209), though Lhermitte does not altogether concur in this view. Recent histological investigations by Spielmeyer indicate that the lesion in the two instances is identical, and that we are not dealing with a pure corpus striatum disease, although the striatal lesion predominates. A peculiar brown-green pigmentation of the periphery of the cornea is described as typical of the disease by German authors, but this has not been recorded in cases diagnosed as progressive lenticular degeneration in this country or in America.

iii. *Presenile and senile pseudobulbar syndromes of the corpus striatum.* A pseudobulbar syndrome of striatal origin is occasionally seen. It is characterized by attacks of uncontrollable laughter and weeping, by dysarthria, aphonia, and dysphagia, and by loss of voluntary and emotional facial movements, muscular rigidity, and fixation of attitude. Involuntary movements are absent. The lesion is that described by the Vogts' as status disintegrationis (*Medical Science*, 1920, **1**, 436; 1921, **3**, 353).

iv. *Presenile and senile Parkinsonian syndromes of the corpus striatum.* These differ from paralysis agitans by the absence of tremor, or rather in its replacement by athetosis or 'torsion spasm' (*Medical Science*, 1920, **2**, 67). Vascular lesions with neuroglial proliferation constitute the disease in these cases.

B. **Pure striatum syndromes (i. e. caudatus and putamen).**

i. *Vogt's syndrome (Little's disease with etat marbré of striatum).* Includes those cases of diplegia in which there are no pyramidal symptoms, but instead, muscular rigidity, involuntary associated movements and bilateral athetosis. The lesion has been described in *Medical Science* in an abstract of the Vogts' papers (1920, **1**, 436; 1921, **3**, 353).

ii. *General rigidity and progressive athetosis.* This differs from the form just described in being acquired and progressive instead of congenital and regressive. The lesion is that called *status dysmyelinatus* by C. and O. Vogt in the papers already referred to. Spiller's dystonia lenticularis (*Medical Science,* 1921, **3**, 355) approximates to this form.

iii. *Huntington's chorea.* Here the involuntary movements are associated with diminution of muscular tone. The lesion is an atrophic cortico-striate degeneration. (C. and O. Vogt.)

iv. *Acute striatal lesions, Sydenham's chorea.* Lhermitte suggests that the symptoms in this disease may in part be striatal in origin.

v. *Vascular lesions of the striatum.* Symptoms of 'hemi-choreo-athetosis' without paralysis in cerebral vascular disease.

C. **Pallidum syndromes.** The clinical picture of paralysis agitans is characteristic of pallidal lesions. According to Ramsay Hunt, the essential lesion in juvenile paralysis agitans is a selective abiotrophic degeneration of the motor cells of the pallidum. The observation lacks confirmation and does not accord with the findings of Lhermitte or the Vogts in the adult form of the disease.

IV. **Synthesis of these syndromes.** The following general observations may be made for all the syndromes. The disorders are purely motor, are not paralytic, and are concerned with muscle tone, voluntary, automatic, and expressive movements. The characteristic muscular rigidity, so different from the true hypertonus of pyramidal tract lesions, is perhaps the most fundamental feature, and with the exception of Huntington's chorea is found in all the striate syndromes. It is the cause of the vicious attitudes and of the slowness and poverty of movement. The general immobility in voluntary movement and the absence of facial gesture and of involuntary associated movements are very striking features of the syndrome. Not less important are the involuntary movements which may be either of the tremor, athetosis, or choreiform variety. There is probably no essential qualitative difference between these three, and the underlying state of muscle tone may be responsible for their differences.

Lhermitte does not discuss in detail the various elaborate and speculative hypotheses as to the functions of the corpus striatum which have been put forward, but contents himself with the general and obvious conclusion that the functions of the corpus striatum are very different from those of the pyramidal system. The latter has to do with highly differentiated movements, the former with more rudimentary automatic movement complexes, such as walking, movements of defence, and of spatial orientation; it is these which are affected by lesions of the corpus striatum.

F. M. R. W.

Wilson, S. A. K. Some problems in neurology: I. The Argyll Robertson pupil. *J. Neurol. & Psychopathol.*, 1921, **2**, 1.

There is still some confusion as to the precise definition of the sign, and Wilson regards it as consisting in the absence, or obvious diminution, of the direct reflex to light, the consensual reflex being either absent or present, with preservation of the pupillary reaction on convergence-accommodation. Myosis is not an essential element in the sign, though some 30 per cent. of cases are also myotic.

Clinical conditions in which it is found. It is a prime neurological principle that symptoms depend more upon the site and mechanisms involved in a lesion than upon its pathological nature, hence, although the Argyll Robertson pupil is present in the majority of cases of neurosyphilis, we should hesitate to regard it as exclusively or certainly syphilitic in origin. Therefore we have to seek for a local action of the spirochaete or its toxin to accord with the occurrence of the sign in non-syphilitic conditions.

The study of the localizing signs in non-syphilitic conditions in which the phenomenon occurs is therefore of primary importance. Among the toxic-infective conditions in which it has been reported is epidemic encephalitis, while there is no doubt that it may occasionally be found in disseminated sclerosis. In certain cases of tumour in the vicinity of the third ventricle, aqueduct, or anterior corpora quadrigemina, an Argyll Robertson pupil may be observed as a stage in the development of complete fixation of the pupils. Such cases afford the most delicate localizing information as to the underlying lesion. The combination of Argyll Robertson pupil with loss of upward movement of the eyes has been observed by Wilson. Among other conditions in which its occurrence has been reliably reported are syringomyelia and syringobulbia, chronic alcoholism, diabetes mellitus, and chronic hypertrophic interstitial neuritis. Finally, a few traumatic cases are recorded.

We cannot deny, therefore, the pathological multiplicity of the sign.

The anatomo-physiological arc for the light reflex. The action of light on the retina is to set in action two distinct physiological mechanisms, the sight mechanism concerned with vision, and the light mechanism concerned with reflex contraction of the pupil. Anatomically, also, the pupillary and visual paths are distinct. The reflex pupillomotor path undergoes a partial decussation at the chiasma and passes back in the optic tract and by the superior brachium to the grey matter of the anterior colliculus. Bilateral section of the superior brachium in apes abolishes the light reflex (Karplus and Kreidl). Ferrier and Turner's early experiments cannot, for reasons given by Wilson, be taken to invalidate this view. The exact anatomical pathway from the colliculus to the sympathetic nucleus in the oculomotor nuclear complex has not been definitely traced. Certain fibres arising in the deepest layer of the colliculus pass as the colliculo-nuclear tract to make an uncrossed and crossed connexion with the oculomotor nuclei in the mid-brain. In doing so they skirt the central grey matter of the aqueduct and would thus be the first fibres to suffer from any periaqueductal toxic invasion.

Wilson discusses at some length other possible paths between anterior colliculi and oculomotor nuclei.

The localization of the iris-constricting centre in the oculomotor nuclei is then further discussed, and he concludes from the evidence that the pupillomotor function commonly ascribed to the Edinger-Westphal nucleus is not settled beyond dispute. It has been suggested that the colliculo-fugal light reflex fibres do not enter the oculomotor nuclei, but pass straight into the oculomotor nerves and thence to the ciliary ganglia.

The path for convergence and accommodation. Accommodation is a willed movement, and therefore of cortical origin. Three muscles take part in it, internal rectus, ciliary muscle, and sphincter iridis. The pathway from the cortex is by the cortico-nuclear tract, through the internal capsule and the pes lemnisci profundus to the extrinsic ocular muscles. From the oculomotor nuclei the pathway for iris contraction in accommodation is the same as that for the light reflex.

Localization of the lesion underlying the Argyll Robertson pupil. From these anatomical data it follows that a single localization for the Argyll Robertson pupil is not to be expected, except that all the evidence places such a lesion on the afferent side of the light reflex arc, that is afferent to the iris-constrictor centre in the oculomotor nucleus.

According to Wilson, by far the commonest localization is in the neighbourhood of the aqueduct, where colliculo-nuclear fibres may be caught before they enter the oculomotor nucleus, and from which accommodation fibres are remote. He lays great stress upon the occurrence of the Argyll

Robertson pupil in cases of tumour in the region of the aqueduct and anterior colliculus in this connexion. This, as Wilson points out, is the view advanced by W. Harris as long ago as 1904. To account for the frequency of the sign in neurosyphilis, Wilson suggests that the syphilitic virus may have a special tendency to filter through the ependyma to affect periaqueductal fibres, especially afferent terminal arborizations. On the basis of such an irregular spread the occurrence of unilateral and of partial defects of light reaction could be accounted for.

The myosis of many Argyll Robertson pupils, Wilson believes to be due to paralysis of the pupillo-dilator mechanism, and he suggests, following some experimental observations of Karplus and Kreidl, that when myosis occurs with Argyll Robertson pupil the irido-dilator pathway is involved somewhere near Meynert's dorsal tegumental decussation, or near the aqueduct.

Various other possibilities and hypotheses are discussed in this interesting and important paper, to which is added a comprehensive bibliography.

F. M. R. W.

MAGNUS, V. Behandling av trigeminusneuralgi med alkoholinjektioner og extirpation av trigeminusroten. [**The treatment of trigeminal neuralgia by injections of alcohol and extirpation of the trigeminal root.**] *Norsk Mag. f. Laegevidensk.*, 1921, **82**, 420–4.

In a review of his own investigations and of the literature of trigeminal neuralgia, Magnus insists that peripheral resection of branches of this nerve has been rendered superfluous and out-of-date by the far simpler device of injecting alcohol. He has resected branches of this nerve 29 times, and all his cases relapsed in a year to 18 months. In 118 cases he gave 248 injections of alcohol, and one of his patients, who was given an injection into the infra-orbital foramen, was free from pain for 8 years. But as with the resections, the average freedom from pain was only for a year to 18 months, and this was so whether the injection was peripheral or basal. While 211 injections immediately induced anaesthesia, 37 proved nugatory, and many of the patients who relapsed after injections, insisted on a radical operation. Magnus has excised the Gasserian ganglion or its pontine root in 31 cases, in none of which did the operation cause ocular paralyses. But in one case transitory facial paralysis was caused by laceration of the large superficial petrosal nerve. There was only one fatality in this series, and though death did not occur till four months after the operation, it probably shortened the patient's life. In four cases Magnus was tempted, after reading J. Hutchinson's book, to perform partial resection of the Gasserian ganglion, i. e. resection of the second and third branches of the nerve together with the adjoining portions of the ganglion. One of these patients relapsed four years later. The object of this partial resection is to avoid trophic disturbances of the eye, but Magnus considers this danger slight compared with that of relapse of the neuralgia. In all his 31 cases, in one of which the neuralgia had lasted 28 years, relief from pain was obtained. Magnus has nothing good to say of injection of alcohol into the Gasserian ganglion itself; he has never had the vicarious courage to attempt this procedure, the literature of which, as he points out, contains records of immediate fatalities, paralyses of the other cranial nerves and meningitis-like symptoms.

C. L.

Kempf. *Psychopathology.* Henry Kimpton, London, 1921, pp. 785.

The book is the author's latest and most ambitious attempt to provide a physiological basis for the Freudian 'wish'. Unhappily, the premise from which he so confidently starts in the construction of his elaborate edifice of theory is one rejected by physiologists. This is the view originating with de Boer and supported by Langelaan that postural muscle tone is a function of the sarcoplasmic element of muscle and derives its innervation from the sympathetic nervous system, and not from the cerebrospinal system. Boeke's histological investigations have revealed the presence of sympathetic nerve endings in striated muscle, but de Boer's interpretation of their function has been confirmed by no subsequent worker and has been impugned by all who have repeated his experiments. In a reasoned account of the evidence for and against de Boer's view, Adrian in this journal (1920, **2**, 454) pointed out that so far from the functions of these sympathetic nerve endings being known, their existence is the only indication that they have any function at all.

However, quite undeterred by the stillbirth of his fundamental assumption, Kempf proceeds with his argument to the following effect; the autonomic nervous system dominates the more recently developed cerebrospinal, or projicient, nervous system, which it employs to secure the gratification of the primitive cravings arising in structures associated with the former. Included in the autonomic system, in addition to what is usually comprehended by the term, are the central nervous paths and centres concerned in the maintenance of postural tonus, that is, the proprioceptive non-sensory reflex system. Among the structures innervated by this extended autonomic apparatus is the sarcoplasmic element of the skeletal musculature, which Kempf regards as the effector organ of skeletal muscle tone.

In the viscera and skeletal structures arise 'primitive autonomic-affective cravings'. It is the duty of the central nervous system to integrate all these peripherally arising cravings and by its activity to satisfy or neutralize them. This is the lofty function of the central nervous system as it stands revealed in Kempf's imagination: it is for this alone that the cerebral cortex of man has been evolved. Hunger cravings arising in the stomach determine a localized postural hypertension in the gastric musculature. The organism becoming aware of this, sets the central nervous system to the task of initiating activities to satisfy this need. Similarly, impulses arising in the muscles influence 'the thought content of consciousness', and 'in a certain sense we think with our muscles'. In view of the radical unsoundness of Kempf's physiological conceptions, further consideration of the far-reaching psychological speculations erected thereon is superfluous. Nevertheless, we cannot refrain from expressing astonishment at the industry with which he and those who agree with him continue to build castles in sand. That clinical psychologists should earnestly seek for a physiological basis for their views is matter for congratulation, but the invoking of physiological factors involves the serious and critical study of physiology, and not merely the forensic selection of such observations as corroborate psychological speculations, the tearing of phrases from their context in physiological papers, and, not less frequently, the complete ignoring of whatever is discordant. Physiology is not a catspaw for the pulling of psychological chestnuts out of the fire. As long as many clinical psychologists continue thus to regard it, so long shall we have to endure the wild speculations and the hopeless confusion of psychological with physiological categories which characterize their writings on the subject. F. M. R. W.

Enghoff, H. **Studies in zoster.** *Acta Med. Scand.*, 1921, **54**, 468–91.

Enghoff's records of several cases of herpes zoster are discussed with special reference to (1) the condition of the cerebrospinal fluid and (2) the hypothesis, advanced in 1907 by Petrén and Bergmark, that a considerable sensory disturbance at the time of a zoster eruption is of ill omen as foretelling a subsequent chronic neuralgia. With reference to the first point, lumbar puncture revealed in one case numerous mulberry-shaped red blood corpuscles, and in another a slight lymphocytosis. The conclusion is drawn from these and other cases recorded by French writers that Head and Campbell are right in regarding zoster as an acute infectious disease. With reference to the second point, Enghoff's findings are inconclusive. One of his cases was certainly confirmatory of Petrén's and Bergmark's hypothesis. The patient was a man of 48, whose zoster dated five years back. The eruption was spread over a 10 to 15 cm. wide area on the right side at the level of the umbilicus. There were also occasional eruptions on the penis, the nose, and the temples. In spite of acute pain one night, he went hunting next day. On the following day his temperature was over 40° C. He was febrile for two weeks and was confined to bed for about five months. The vesicles, which became as large as grapes, did not heal till the fourth month. Though relieved, the pain did not cease altogether, and after five years was still violent whenever he performed certain movements or placed himself in certain positions.

In another case, however, cervico-thoracic zoster was accompanied by considerable sensory disturbances manifested by hypoalgesia, analgesia, and relatively slight neuralgia. In spite of the patient's age (63) and the considerable sensory disturbances, complete cure was effected by diathermy in a short time. In one case zoster on the right side of the back and abdomen immediately above the umbilical region was followed by sciatica on the right side, and Enghoff refers to a similar case recorded in 1911 by Tinel. C. L.

Amantea, G. Über experimentelle beim Versuchstier infolge afferenter Reize erzeugte Epilepsie. [**Experimental epilepsy excited by afferent stimuli in animals.**] *Arch. f. d. ges. Physiol.*, 1921, **188**, 287.

About 25 per cent. of normal dogs exhibit a hyperexcitability of the motor cortex to unipolar stimuli, and in these (but not in normal) dogs, typical epileptic seizures may be produced by stimulation of the skin when the sensori-motor cortex of the corresponding area of the cerebrum has been rendered still more excitable by local application of 1 per cent. strychnine. The attack commences in those muscles the motor centres of which have been treated with strychnine. After strictly local cauterization of the treated centres, stimulation of the reflexogenous skin zone is ineffective. Stimulation of these before applications of strychnine to the centre is also ineffectual. C. L. E.

PATHOLOGY AND BACTERIOLOGY

Wolf, F. A., and Shunk, I. V. Solid culture media with a wide range of hydrogen or hydroxyl-ion concentration. *J. Bact.*, 1921, **6**, 325.

The purpose of this paper is to show that acids and alkalis need not materially modify the physical properties of agar and gelatin media within, and even far beyond the limits of tolerance of any living organism. The media were prepared by adding 1 or 2 per cent. agar or 10 or 15 per cent. bacto-gelatin to a bouillon consisting of 0·3 per cent. Liebig's beef extract, 1 per cent. Armour's peptone, and 0·5 per cent. sodium chloride, and then autoclaved. Two tables of results are given. The first shows the effect of acid (HCl) and alkali (NaOH) on the solidification of agar. The second substitutes gelatin for agar. In the case of both agar and gelatin, strong acid or alkali in the presence of high temperatures can destroy jellifying power. The approximate P_H limits were 1·4 and 9·2. Details are given to show how to avoid contamination during the adjustment of the reaction so that no subsequent sterilization is required. W. A. M. S.

Thjötta, Th., and Avery, O. T. Studies on bacterial nutrition. II. Growth accessory substances in the cultivation of hemophilic bacilli. *J. Exper. M.*, 1921, **34**, 97.

Attention has already been directed (*Medical Science*, 1921, **4**, 562) to the research of Thjötta who believed he had proved that *B. influenzae* will grow on a haemoglobin-free medium consisting of plain broth enriched by sterile suspensions or extracts of mucoid bacteria. In the present paper this study has been carried farther, and an attempt is made to determine the growth requirements of haemophilic bacilli and to indicate the significance of growth accessory substances in bacterial nutrition. The first experiments were made with extracts prepared from yeast cells and from fresh tomatoes, green peas, and beans. It was found that *B. influenzae* will grow when transferred by a small inoculum from blood media to plain broth containing extracts of the above substances, although it fails to grow under the same conditions in the same broth devoid of these substances. No growth, however, was obtained progressively in broth containing only yeast or vegetable extracts. The enriching substances in the extracts were found to resist boiling for ten minutes, but were rendered inert in the autoclave at 120° C. for 30 minutes. Further examination showed that they contain but little available nitrogen, traverse Berkefeld filters with little or no loss, but are adsorbed from water when brought into contact with animal charcoal. Turning to the question of the influence of blood which has always been regarded as a necessity for the growth of *B. influenzae* the authors find evidence not only of a vitamine factor *V*, but of another factor *X*, and it is the combination of these which makes blood-containing media so satisfactory for *B. influenzae*. The substance *X*, to the lack of which influenza bacilli are peculiarly sensitive, is capable of acting in excessively minute quantities although it is unable to functionate by itself. The *V* factor is destroyed by heat at 120° C. while the *X* factor remains unimpaired. Both survive a temperature of 100° C. for ten minutes. Extracts expressed from the coagulum of boiled blood contain both principles, whereas autoclaved blood contains only *X*. Both principles are present in greater concentration in the cellular elements of the blood than in the plasma or serum. The red blood cell appears to be the carrier of the vitamine-like principle *V* whereas the *X* principle is intimately associated with, or a derivative of, the haemoglobin only. It was found that the *X* factor can functionate in a dilution of 1 : 2,000,000 provided that there is a liberal supply of the *V* factor. Similar conclusions were reached by Fildes (*Brit. J. Exp. Path.* 1921, **2**, 16). W. B.

Plimmer, H. G., and **Paine, S. G. A new method for the staining of bacterial flagella.** *J. Path. & Bacteriol.*, 1921, **24**, 286.

The method was invented by the late Dr. H. G. Plimmer, some of the details being worked out by S. G. Paine. The stain is made as follows:

Tannic acid 10 gm.
Aluminium chloride (hydrated) 18 gm.
Zinc chloride 10 gm.
Rosanilin hydrochloride 1·5 gm.
Alcohol 60 per cent. 40 c.cm.

The solids are placed together in a mortar and immediately triturated with the alcohol. Ten c.cm. of the alcohol are used first and the mass is mixed thoroughly, the rest of the alcohol being stirred in slowly till the mass goes gradually into a viscous solution of a deep red colour. The solution apparently remains stable for years. For use it is diluted with water when nearly complete precipitation occurs, a small amount remaining in solution.

The usual precautions for successful flagella staining must be observed. No fixation is required. One part of the stain, say 0·5 c.cm., is mixed with 4 parts of water and allowed to stand for one minute, after which it is filtered directly on to the film and again allowed to stand for one minute when a slight bronzing is visible on the surface. It is then washed under the tap. The film is then flooded with cold carbol fuchsin for five minutes, dried and examined in oil, and if satisfactory is mounted in balsam or euparal. The preparations are permanent.

A high percentage of successful results are claimed for the method, the background being relatively or absolutely free of deposit. W. B.

Cross, H. B. A contribution to the staining of phagocytes and exudates. *Johns Hopkins Hosp. Bull.*, 1921, **32**, 51.

The author recommends the following stain for phagocytes and exudates:

Distilled water (neutral)	100 c.cm.
Glycerol . . .	20 ,,
Alcohol (95 per cent.)	20 ,,
Phenol . . .	2 ,,

To this is then added

Crystal violet	0·060 gm.
Pyronin	0·200 ,,

Solution rapidly takes place and the stain is ready for use without filtering. It is stable if protected from sunlight and evaporation.

Films are made and allowed to dry in air without heat or other fixation.

Stain takes place in 5 to 10 seconds after which the preparation is washed with distilled water, any excess of water is mopped up with blotting paper, but the film itself should not be blotted.

The cell nuclei are stained violet and the cytoplasm of a uniform delicate lavender, the cell limits being well defined. Bacteria are a deep purple. Erythrocytes appear as pale lavender shadows. Plasma cells and mast cells exhibit a characteristic structure and stain darkly throughout so that they are easily recognized. W. B.

Topley, W. W. C., and **Weir, H. B. The lesions produced in rabbits by the inoculation of streptococci isolated from rheumatic and other lesions in the human subject.** *J. Path. & Bacteriol.*, 1921, **24**, 333.

This paper describes the effects on a considerable number of rabbits of the injection of cultures of streptococci obtained from various sources, but especially from ulcerative endocarditis. In one case a streptococcus was isolated *post mortem* from a boy aged 16, dead from cardiac disease consequent on a febrile disease with joint pains some months previously. In a large number of cases joint lesions developed with or without streptococci. Endocardial and myocardial lesions were observed and in one case, appendicitis. The authors discuss the theories with regard to the aetiology of rheumatic fever, and while not committing themselves, they think that the view that the presence of streptococci is accidental or unimportant, or that it is merely one of several organisms which give rise to secondary infections in the course of the disease seems difficult to reconcile with all the ascertained facts. They admit, however, that lesions similar to those produced by inoculation of streptococci from rheumatism may be produced with streptococci obtained from sources quite unconnected with rheumatic infection, a fact which was clearly demonstrated by Loeffler in 1884 (*Mitth. a. d. K. Gesundheitsamte*, 1884, **2**, 457) in the course of his investigations on diphtheria. W. B.

Olitsky, P. K., and **Gates, F. L. Experimental studies of the nasopharyngeal secretions, from influenza patients. V. Bacterium pneumosintes and concurrent infections.** *J. Exper. M.*, 1921, **34**, 1.

The researches of the authors have already been referred to (*Medical Science*, 1921, **4**, 266). From the nasopharyngeal secretions of patients in the early hours of an attack of uncomplicated influenza and from the lungs of rabbits and guinea-pigs inoculated with such secretions they found an anaerobic filter-passing bacilloid organism which they called *Bacterium pneumosintes*. The present paper is a study of the ability of this agent to reduce pulmonary resistance in animals and bring about infection with ordinary bacteria, as, the authors believe, may occur in influenza. For this purpose rabbits were first inoculated intratracheally with *B. pneumosintes*, being subsequently injected intratracheally or intravenously with cultures of *B. influenzae* or *Pneumococcus* Type IV in subinfective doses. The result was a consolidation of the lungs with polynuclear exudation combined with the haemorrhagic oedema and emphysema which the authors consider to be the typical lesion induced by *B. pneumosintes*. Control animals injected with the latter organism alone showed only haemorrhagic oedema and emphysema but without pulmonic consolidation. From this the authors conclude that the lungs of animals infected with *B. pneumosintes* are less resistant than normal lungs to infection with ordinary bacteria. W. B.

Pilot, I., and **Pearlman, S. J.** (1) **Bacteriologic studies of the upper respiratory passages. I. Hemolytic streptococci of the adenoids.** *J. Infect. Dis.*, 1921, **29**, 47.

Pilot, I., and **Pearlman, S. J.** (2). **II. The pneumococci and non-hemolytic streptococci of the adenoids and tonsils.** *J. Infect. Dis.*, 1921, **29**, 51.

Pilot, I., and **Pearlman, S. J.** (3). **III. The influenza bacilli (Pfeiffer) of the adenoids and tonsils.** *J. Infect. Dis.*, 1921, **29**, 55.

Meyer, J., Pilot, I., and **Pearlman, S. J. IV. The incidence of pneumococci, hemolytic streptococci and influenza bacilli (Pfeiffer) in the nasopharynx of tonsillectomized and non-tonsillectomized children.** *J. Infect. Dis.*, 1921, **29**, 59.

Pilot, I. V. The diphtheria bacilli and diphtheroids of the adenoids and tonsils. *J. Infect. Dis.*, 1921, **29**, 62.

These five researches were carried out in the Department of Pathology and Bacteriology of the University of Illinois, Chicago, and are concerned with a study of bacteria in extirpated adenoids and tonsils. The first paper deals with haemolytic streptococci obtained from the adenoids of 103 children. Twenty-five cases being examined by means of swabs while the remaining 78 examinations were made from excised specimens. For nasopharyngeal swabs and the surface of adenoids haemolytic streptococci were recovered in 55 per cent. and from the depth and crypts in 61 per cent., while the excised tonsils of the same patients showed similar cocci in no less than 95 per cent. of the cases examined. The authors conclude that like the tonsils, adenoids harbour haemolytic streptococci showing complete analogy with those from various human sources. In the second paper pneumococci and non-haemolytic streptococci are investigated. In 103 adenoids pneumococci were found in 65 per cent., 2 per cent. being of Type II, 13 per cent. of Type III, and 85 per cent. of Type IV. In the nasopharyngeal swabs of 21 persons pneumococci were found in 71·4 per cent., from the tonsils in 66·6 per cent., and in adenoids in 71·4 per cent. *Streptococcus viridans* was found in 89 per cent. of the adenoids and in 81 per cent. of the tonsils. *S. mucosus* was found in 3 per cent. and indifferent streptococci in 12 per cent.

Continuing their researches the authors, in their third paper, deal with the incidence of influenza bacilli in the adenoids and tonsils of 115 persons at ages varying from 5 to 16 years. Positive results were obtained in 40·9 per cent. of extirpated adenoids and in 53·9 per cent. of tonsils. In 25 instances nasopharyngeal swabs were examined and haemoglobinophilic bacteria were found in 40 per cent.

In the fourth paper a comparison is made between the incidence of certain bacteria in children with or without their tonsils. Pneumococci, haemolytic streptococci, and *B. influenzae* were frequently found in normal children. The incidence and numbers of haemolytic streptococci and influenza bacilli in the nasopharynx were found to be decidedly less in the children whose adenoids and tonsils had been removed.

In the case of pneumococci the numbers were less in the same children than in those whose tonsils had not been removed. The removal of tonsils and adenoids reduces the number of certain bacteria in the oropharynx and nasopharynx, but does not cause their disappearance.

The fifth and last paper of the series deals with the incidence of diphtheria and diphtheroid bacilli in material obtained from 100 children 5–15 years of age, who entered hospital to have their tonsils and adenoids removed chiefly on account of hyperplasia. None of them had acute inflammation of the throat and no reliable history of diphtheria could be obtained in any case. The histological examination of the tonsils and adenoids after removal showed no marked change other than hyperplasia. From 100 cases of such adenoids and tonsils the author recovered diphtheria bacilli in 12. In the crypts of the tonsils the bacilli were more numerous than in the corresponding adenoids. Where bacilli were found in the tonsils they were also found in the adenoids. The virulence and fermentative properties, of the diphtheria bacilli isolated, were examined. Two were found to be virulent, in doses of 1, 2, and 3 c.cm. of a broth culture, for guinea-pigs causing death in 24 hours. One strain showed low virulence while three others in doses of 5 c.cm. were at first slightly virulent and later, avirulent. Six strains were non-pathogenic for guinea-pigs. In 1 per cent. carbohydrate broth with Andrade indicator all the twelve strains produced acid in dextrose and dextrin, 10 in maltose and lactose, but none fermented saccharose and mannitol.

Diphtheroid bacilli appearing as non-granular short rods were found in 30 per cent. of the adenoids and in 17 per cent. of the tonsils examined. When present in both they were decidedly more numerous in the nasopharyngeal vegetations than in the tonsillar crypts. Twenty pure cultures of the diphtheroids isolated failed to ferment dextrose, lactose, maltose, saccharose, or dextrin. W. B.

Tunnicliff, Ruth. Observations on the spread and persistence of the hemolytic streptococci peculiar to scarlet fever. *J. Infect. Dis.*, 1921, **29**, 91.

The authoress has previously described certain haemolytic streptococci isolated from early cases of scarlet fever and its complication, and has shown that these micro-organisms are apparently peculiar to the disease in that they are specifically opsonized and agglutinated by the serum of a sheep immunized with a haemolytic streptococcus obtained from scarlet fever. The present paper deals with the streptococci from the rooms, eating utensils, and attendants of diphtheria and scarlatinal patients to see if they belong to the same group as those indicated above. The serological tests were carried out with the serum of a sheep which had been immunized over a period of eight months. Twenty strains of haemolytic streptococci were isolated from the floor and walls of rooms occupied by patients with scarlatina and diphtheria and from the finger-nails, face-masks, and shoes of nurses, and from the eating utensils used by patients harbouring haemolytic streptococci. From the opsonic and agglutinating reactions five of the twenty strains agreed with those believed to be specific for scarlet fever, four of them being isolated from the eating utensils of scarlet fever patients and one from the face-mask of a nurse in attendance. Haemolytic streptococci were isolated from ten hospital attendants who had tonsillitis, from the throats of three healthy nurses, one a diphtheria nurse and the other two, scarlet-fever nurses, from the infected fingers of two medical residents, and from the C. S. F. of a case of meningitis following tonsillitis. Only two of the strains were of the scarlet-fever type, one being obtained from the throat of a ward-maid with acute tonsillitis, the other from the throat of a scarlet-fever nurse. Neither of them had a rash. With regard to the persistence of scarlet-fever streptococci the authoress finds that while, as a rule, they are present from three to five weeks after the onset of the disease they may persist longer in patients with discharges from the nose and ear, and disappear at the time when, according to clinical experience, the patient is no longer infective. W. B.

Cronstedt, L. A study of the so-called parameningococci. *J. Path. & Bacteriol.*, 1921, **24**, 211.

The author examined thirteen strains of meningococci which were obtained from soldiers who had been in contact with a case of cerebrospinal meningitis, although cultures from the latter were not obtained. The thirteen strains fermented dextrose and maltose, while laevulose, lactose, galactose, mannitol, &c., were left unaffected. Agglutinating reactions were made with four sera, of which one was prepared from a typical strain of meningococcus, one from one of the thirteen strains, two other sera being polyvalent. Such striking differences and variations were obtained in the agglutinating tests that the author considers that the differentiation of parameningococci appears to be ill-founded. W. B.

Meyer, K. F. I. Experimental typhoid-paratyphoid carriers. *J. Infect. Dis.*, 1921, **28**, 381.

Schoenholz, P., and **Meyer, K. F. II. The optimum hydrogen-ion concentration for the growth of *B. typhosus* and *B. paratyphosus* A and B.** *J. Infect. Dis.*, 1921, **28**, 384.

Christiansen, C. R., Neilson, N. M., and **Meyer, K. F. III. Do 'carrier' strains differ from strains isolated from ordinary typhoid cases?** *J. Infect. Dis.*, 1921, **28**, 394.

Meyer, K. F., and **Neilson, N. M. IV. A comparative study of the infections produced by intravenous injections of typhoid, paratyphoid A and B bacilli in normal and immunized rabbits.** *J. Infect. Dis.*, 1921, **28**, 408.

Meyer, K. F., Neilson, N. M., and **Feusier, M. L. V. The mechanism of gall-bladder infections in laboratory animals. [B.]** *J. Infect. Dis.*, 1921, **28**, 456.

Neilson, N. M., and **Meyer, K. F.** (1). **VI. The reaction and physiology of the hepatic duct and cystic bile of various laboratory animals. [B.]** *J. Infect. Dis.*, 1921, **28**, 510.

Neilson, N. M., and **Meyer, K. F.** (2). **VII. The bacteriostatic and germicidal properties of bile.** *J. Infect. Dis.*, 1921, **28**, 542.

Schoenholz, P., and **Meyer, K. F. VIII. The influence of the H-ion concentration of the growth of *B. typhosus* in mediums containing bile or bile salts.** *J. Infect. Dis.*, 1921, **28**, 588.

These papers constitute a part of an extensive experimental research on typhoid infection carried out by K. F. Meyer and various collaborators in the Medical School of the University of California. The first paper is short and explanatory of the programme followed in the various studies. In the second the optimum H-ion concentration for typhoid bacilli is investigated, the authors finding that the microbe has a range of growth from $P_H + 5{\cdot}0$ to $P_H + 8{\cdot}6$ with an optimum growth at $P_H + 6{\cdot}8$ to $P_H\ 7{\cdot}0$ in a salt-free veal infusion broth. Above or below these limits the resulting growth in comparison is very slight. Large variations in the H-ion concentration near the optimum zone produce only slight effects on the growth of the organisms, while slight variations at the limiting zone produce a marked effect. Stock cultures isolated from stools, blood, and urine of typhoid patients, or carriers, have a more decided optimum than recently isolated cultures. In such cultures the plateau of the growth curve is much more pronounced and extends over a wider range than in stock cultures. *B. paratyphosus* A and B have a range of growth at varying H-ion concentrations similar to that of *B. typhosus*, but exhibit a greater tolerance for alkalis than *B. typhosus.*

The third study was undertaken to elucidate certain facts recorded in the literature pertaining to animal carriers. A comparative examination on fourteen carrier strains failed to reveal any striking differences between such strains and those isolated from acute cases of enteric fever. Seven carrier strains tested on rabbits by means of intravenous inoculations failed to exhibit specific elective cholecystotropic or renotropic properties. Further, it was impossible to induce such properties in a recently isolated strain of *B. typhosus* when it was passed through the gall-bladders of rabbits. It appears, however, that immunized rabbits inoculated with large doses of living typhoid bacilli exhibit infections in the gall-bladder in a somewhat higher percentage than in normal rabbits.

The fourth paper deals particularly with the fate and disappearance of typhoid and paratyphoid bacilli traced from the blood through the various organs. A small number of typhoid bacilli inoculated intravenously into normal rabbits of the same litter disappeared from the blood-stream at the end of 10 or 15 minutes after the inoculation. About 20 to 30 per cent. of the inoculum was found in the liver, a smaller amount in the spleen, marrow, and lungs. Comparatively few bacilli were recovered from the lymph nodes, kidneys, muscle, &c. The bile from the gall-bladder contained only small numbers of bacteria, whereas the wall of the gall-bladder had received according to its size a proportionate share of the total number of bacteria deposited in the liver. Injection into the portal system from a mesenteric vein presented no obvious advantage over the ordinary injection into the aural veins. When a large dose of bacilli is injected it disappears less readily from the circulation, although the distribution in the organs remains the same during the first 4 to 8 hours. Examination showed that the bacilli taken up by the tissues are rapidly reduced in number, especially in the liver, spleen, and lungs. The bone-marrow appears to be less active, and not infrequently the typhoid bacilli multiply there and form foci which cause a reinfection of the blood-stream. The gall-bladder may become infected either as a result of an immediate extensive elimination of the bacteria injected or through the continuous discharge of bacilli from liver foci in the hepatic bile, or in consequence of an embolic infarction of the capillaries of the wall of the gall-bladder inducing a diphtheritic cholecystitis. In the latter instance the bile of the gall-bladder itself may not become invaded with typhoid bacilli for 24 to 48 hours after the intravenous injection. When similar injections were made on actively immunized rabbits the results were essentially the same, except that the lung of the immunized animal takes up a somewhat greater number of bacteria than the normal animal and the spleen of the immune animal sterilizes itself more slowly than the normal. Rabbits which succumb to the typhoid intoxication, regularly harbour enormous quantities of bacilli in the marrow of the long bones, the authors considering that foci in this locality are probably the seed beds responsible for the continuous invasion of the blood-stream and the subsequent overwhelming infection of the liver and spleen.

Paratyphoid A bacilli act in a manner identical with typhoid bacilli. The mechanism of destruction of *B. paratyphosus* B both in the normal and in the immunized rabbit differs from that found in the case of *B. typhosus*. As a rule, paratyphoid bacilli disappear more quickly from the blood and tissues of immunized than normal animals. The authors found also that the blood and serum of normal rabbits *in vitro* is bacteriolytic for typhoid and paratyphoid A bacilli, but is inactive for paratyphoid B bacilli. The serum of immunized rabbits, *in vitro* whether protected against typhoid, paratyphoid A or B was found not to be bactericidal. Pieces of excised organs of exsanguinated rabbits, heavily infected with bacilli of the typhoid-paratyphoid group, when incubated in test-tubes at 37° C. may show in the first two hours a slight bactericidal action, especially in the lung. The bactericidal property is dependent on the living protoplasm of the cells as it is not manifest in extracts.

The fifth paper deals with the mechanism of gall-bladder infections and contains a good critical review of the literature on the subject. A technique is described for obtaining bile from the hepatic duct. The elimination of typhoid bacilli in the bile of the hepatic duct was studied in normal and immunized rabbits, guinea-pigs, and dogs with temporary fistulae of the common duct. It was found in the case of the rabbit that more bacteria appear in the bile of normal animals injected intravenously with 8,000 to 24,000 million bacilli than in that of immunized animals of the same litter, provided the last inoculation of the vaccine is made 20 to 30 days previous to the intravenous inoculation. By the descending or haemo-hepatogenous route the elimination is immediate, the maximum number of bacteria developing on the plates within 15 minutes of the injection. In subsequent periods the number of bacilli decreases rapidly and the discharge of bacteria in the bile may be completed by the end of one hour. The ability of the rabbit to eliminate bacteria varies, however, with the individual, some animals never having this property at all. The authors were led to the conclusion that the transit of the bacilli from the hepatic blood-vessels to the bile capillaries is probably governed by the phagocytic action of the endothelial cells. Immunization of the rabbits prevents, to a certain extent, the passage of the bacilli. In the immunized guinea-pig the endothelial barrier is exceedingly efficient, and an intravenous injection of less than 100 million typhoid bacilli does not lead to any discharge of bacilli in the bile, whereas in normal guinea-pigs several hundred bacilli in the intravenous inoculation is sufficient to cause the appearance of some of them in the hepatic duct bile. Rabbits inoculated with dead or living typhoid bacilli and then injected intravenously with living bacilli on the 6th–10th day after the last immunizing injection discharge more bacilli than normal control animals of the same litter. The authors consider that this is probably due to an incomplete *restitutio ad integrum* of the altered vascular endothelium. When complete recovery has taken place the bacilli are prevented from entering the bile. In dogs the excretion of typhoid bacilli in the hepatic bile is irregular and seems to have no reference to immunization. The disappearance of typhoid bacilli and leucocytes from the peripheral bloodstream was also investigated, the leucopenia being attributed to an uneven distribution of the leucocytes which are chemotactically attracted to the bacillary masses collecting in the viscera. In the course of nearly 500 necropsies on rabbits infected by intravenous injection of typhoid bacilli extensive inflammatory processes in the wall of the gall-bladder were found in about 25 per cent., the lesions developing between the 6th and the 72nd hour. During that period necroses and diphtheritic foci were found in the villi of the mucous membrane. The bile in the gall-bladder may be sterile although the wall of the viscus contains thousands of typhoid bacilli. The transverse route of bile infection through the wall of the gall-bladder was also found to occur after ligature of the cystic duct. Injections made directly into the gall-bladder induce an infection along the lymphatic system of the mucosa, submucosa, and subserosa. The epithelium remains intact and there are no focal necroses of the villi of the gall-bladder. With regard to the factors responsible for the persistence of typhoid bacilli it was found that rabbit typhoid carriers may be subdivided into those that are temporary or convalescent and those which are chronic. 30 to 40 per cent. of intravenously inoculated animals recover in a month; whereas 10 to 15 per cent. may retain the bacilli in the gall-bladder for six months or a year or more. The persistence of the carrier state depends on the degree of inflammation in the gall-bladder. The authors believe that chronic carriers probably result from embolic, capillary invasion of the wall with subsequent transverse infection of the bile. Persistence is also favoured by the formation of gall-stones, by the existence of the inflammatory process to the cystic ducts, and by severe cholecystitis and empyema. Calculi which occur in 60 to 80 per cent. of the cases are composed of bilirubin-calcium material. Gall-bladder infections can also be produced by the inoculation of typhoid bacilli into the spleen and into the gall-bladder containing gall-stones.

The sixth paper deals with the reaction and physiology of the bile from the hepatic and cystic ducts in various laboratory animals. The hepatic duct bile of rabbits was constantly found to be alkaline to litmus and frequently also to phenolphthalein, the P_H varying between 7·4 and 7·7 when the examination was made immediately on removal of the bile from the body. The H-ion concentration decreases steadily on exposure to air and may reach a P_H of 9·2, a result probably due to escape of CO_2 and the absorption of ammonia. The reaction of the bile from the gall-bladder is variable. It may be acid, neutral, or alkaline, but is always acid to phenolphthalein. Fasting and acid-forming diets produce cystic biles of a high H-ion concentration. Biles from the hepatic duct or of the cystic duct in guinea-pigs differ but slightly in reaction, but considerably in the dog, cat, goat, and monkey. Bile obtained from rabbits infected with typhoid or paratyphoid bacilli or with streptococci are alkaline to litmus, and 50 per cent. are also alkaline to phenolphthalein. The rate of flow of bile and the influence of cholagogues were also investigated. Experiments on rabbits and guinea-pigs showed that the average hourly output was 10 c.cm., the daily output representing $\frac{1}{8}$ to $\frac{1}{10}$ of the total body-weight of the animal.

The seventh paper is a study of the bacteriostatic and germicidal properties of bile. After an extensive analysis of the literature on the action of bile on bacteria the authors describe their own experiments, which were performed with samples of bile from rabbits, guinea-pigs, dogs, cats, goats, rats, monkeys, cattle, pigs, sheep, and man. Hepatic duct bile of rabbits and guinea-pigs showed selective germicidal properties. Bacilli of the typhoid-paratyphoid-dysentery group were found alive after a sojourn of 72–120 hours and *V. cholerae* and *Staphylococcus* after 7–10 days in bile. Gall-bladder bile collected from the same animals and tested under the same conditions failed to show germicidal properties up to 10 days. Similar conditions were found to prevail in the dog. In cats, goats, rats, and monkeys no bacteriostatic or antiseptic action was found with hepatic duct bile. The authors believe that the germicidal properties of hepatic duct bile of rabbits and guinea-pigs is not due to bacteriolysins or a 'substance sensibilisatrice'. No agglutinins were found. On the other hand, about 25 per cent. of specimens of gall-bladder bile from immune rabbits may contain agglutinins. Recovered carriers may also give clumping with *B. typhosus* in dilutions of 1:100. The authors believe that the degree of the inflammatory process and the stasis in the gall-bladder are factors which conduce to the presence of agglutinins. Elaborate experiments were made to determine the factors which determine the germicidal action of bile. Among these the H-ion concentration of the hepatic duct bile was found to be only indirectly responsible for its antiseptic properties. Dilution of bile with distilled water or sterile serum prolongs the persistence of viable bacteria for several days. The possible growth-enhancing action of 'vitamines' is discussed and rejected. Antiseptic rabbit bile sealed in collodium and placed in the peritoneal cavity of guinea-pigs was found to be an excellent medium for the growth of *B. typhosus.* The rate of growth of *B. typhosus* in ox and in dog bile is discussed. Fresh, unheated, sterile cystic ox bile was found to develop germicidal powers on incubation and exposure to air. During the first two hours a certain number of the viable *B. typhosus* and *B. dysenteriae* are prevented from growing and a large number are destroyed. This period is followed by a lag of varying length which in turn is succeeded by a rapid proliferation, the maximum development being reached on the 12th or 48th hour for the specimen exposed to air. Progressive destruction, however, sterilizes these specimens in 12 to 120 hours, the time varying according to the sample of bile. Ox bile prevented by stratification with oil from giving off CO_2 or from absorbing ammonia in a desiccator does not become germicidal. Old, heated or unheated ox bile acts in a characteristic manner on *B. typhosus.* Immediately after inoculation of the bile a marked destruction of viable organisms takes place which may lead to complete sterilization or is followed by a pronounced lag. This in turn is succeeded by a slow but progressive multiplication of the typhoid bacilli, a multiplication which may reach a maximum only after seven days, at which time the number of bacilli may exceed those in a broth culture. This behaviour of old, heated cystic bile is apparently not connected with the H-ion concentration. The authors consider that sterilized ox bile is unsuitable for the primary isolation of *B. typhosus* from tissues or secretions. Mixed with peptone and glycerol it is, on the other hand, a good medium for typhoid blood cultures on account of its haemolytic properties. In conclusion, the rate of growth of *B. typhosus* and *V. cholerae* in human cystic bile at varying H-ion concentrations was also investigated, the authors suggesting that a large series of such biles should be investigated to determine the actual importance and influence of the secretion as such on the human typhoid carrier state.

The eighth paper is concerned with the influence of the H-ion concentration on the growth of typhoid bacilli in media containing bile or bile salts, and is illustrated by a series of curves. One strain of *B. typhosus* was used throughout the experiments. It was found that ox bile, hepatic duct rabbit bile, 'bacto' desiccated ox bile, sodium glycocholate and taurocholate in 1 per cent. concentration in a 0·01 per cent. 'Difco' peptone phosphate solution at a P_H 7·0 are growth enhancing for *B. typhosus*, while larger amounts such as 3 per cent. to 30 per cent. greatly impede proliferation. At P_H 8·4 the same bile specimens or their salts acquire inhibitory, bacteriostatic, or bactericidal properties. The more concentrated the media are in bile salts the greater is their effect on bacteria. Even small amounts such as 0·5 per cent. destroy inoculated bacteria in 24 hours. At P_H 8·4 glycocholates are more antiseptic than taurocholates. With regard to the practical use of bile and bile-salt media the authors consider that they are advantageous only in neutral or slightly acid substrate and when the concentration does not exceed 1 per cent. or 0·5 to 1 per cent. desiccated ox bile. The value of bile additions to media should not be over-estimated mainly on account of the comparatively slight, stimulating, selective effect on *B. typhosus*, and on account of the production of a distinct lag which is provoked by fairly small amounts of bile salts. W. B.

Nichols, H. J. The production of CO_2 by the typhoid bacillus and the mechanism of the Russell double sugar tube. *J. Infect. Dis.*, 1921, **29**, 82.

Some years ago Russell recommended a double sugar medium containing 1 per cent. lactose and 0·1 per cent. glucose with litmus as an indicator, although Andrade's and fuchsin indicator can also be used. When distributed into tubes in such quantities that when sloped a butt of solid agar one inch deep remains at the bottom of the tube, this medium has been employed in the differentiation of members of the typhoid-colon group. By a stab inoculation into the butt of agar and a streak on the sloped part it is found that if the organism is a lactose fermenter the whole agar to the top of the slope will be red. If the organism is a glucose but not a lactose fermenter the red colour will be apparent round the stab in the butt only. If not a glucose fermenter no colour will develop. According to Russell the entire point of the medium rests upon the difference in changes produced by the growth of the typhoid bacillus under aerobic and under the imperfect anaerobic conditions found in the butt of the tube where the bacillus obtains its oxygen by breaking down the glucose with the liberation of considerable acid; on the sloped surface, however, in the presence of free oxygen, no acid is produced.

The present author has shown that a small amount of acid might be formed in the 0·1 per cent. of glucose and being volatilized might leave the medium unaffected. In an inoculated double sugar tube sealed by heat or paraffin he found that the slant became acid. When an inoculated double sugar tube is coupled up in a tight system with an uninoculated tube the slant of the second tube becomes acid as well as the first, indicating that some volatile acid passes over to the uninoculated tube. He found also that typhoid bacillus ferments glucose in the slant under aerobic conditions, and this is particularly evident when the glucose is present in 0·3 per cent. or more. The volatile acid acts very much like CO_2, and in fact the appearance of a litmus double sugar tube can be exactly duplicated by saturating sterile medium with CO_2. By the use of the tube recommended by Eldredge and Rogers (1914) the author considers he has in fact demonstrated the production of carbonic acid from glucose and from proteins by the typhoid bacillus, and he therefore considers that the appearance of the Russell double sugar tube during the growth of *B. typhosus* is due not to direct oxygen requirements but to retention of CO_2 in the butt of the tube and its escape from the slant and to alkaline reversion of other acids.

W. B.

Koser, S. A. Trehalose fermentation in the differentiation of the paratyphoid-enteritidis group. *J. Infect. Dis.*, 1921, **29**, 67.

In investigating certain bacteria associated with food poisoning the author found that they can be differentiated by their ability to ferment trehalose. This is a disaccharide consisting of two molecules of glucose attached in such a way that both aldehyde groups have disappeared. Two samples of this sugar were tested, the one from a commercial firm, the other from the Carbohydrate Laboratory of the Bureau of Chemistry. Both gave identical results. It was found that *B. suipestifer* is unable to ferment trehalose, whereas *B. paratyphosus* A, *B. Schottmülleri* (*B. paratyphosus* B), *B. enteritidis*, and the 'animal para B' sub-group of Ten Broeck all cause acid and gas formation. Further, the author states that it is possible to differentiate by cultural methods *B. Schottmülleri* from the closely allied 'animal para B' group hitherto separable only by serological methods. This was accomplished by employing small quantities of a serum water medium containing 0·5 per cent. trehalose and 1 per cent. of Andrade indicator. After 3 or 4 days' incubation at 37° C., the coagulum produced by the 'animal para B' cultures presents a deep pink or red colour, while that of the *B. Schottmülleri* cultures is colourless or of a light pink tint. This distinction was found to run parallel to the differentiation of the two groups by agglutinin absorption tests. *B. enteritidis* is similar in reaction to the 'animal para B' cultures. W. B.

Morishima, K. Variations in typhoid bacilli. *J. Bact.*, 1921, **6**, 275.

This is an elaborate investigation carried out upon 138 strains of *B. typhosus*, the object being to determine whether variations which have been described are to be regarded as mutations in the botanical sense, and to contribute to the comprehension of the nature and permanence of variations from type so often noticed in freshly isolated cultures. The author believes that inoculation of a small number of strains into fluid media containing various carbohydrates and recording the production of acid and gas after a few days' incubation is quite inadequate. A large number of strains must be employed and the period of observation extended for a month. Fermentation is to be regarded as the utilization of the sugar as a food by the bacterium and not merely as the production of acid and gas or even acid alone. In this sense, fermentation is conclusively demonstrated if characteristic 'daughter' colonies appear on agar containing the sugar, and no 'daughter' colonies appear on plates of the same agar without the sugar. By studying a large number of strains, the individual observations extending over several weeks, the author noted that the behaviour of many strains towards certain sugars varied widely from that of other strains. The slow fermenters of xylose resemble the mutations of higher plants more closely than some of the other variants because they retain their characteristics for years so long as they are not grown in xylose broth. All the slow xylose fermenters, including one which never produced acid in xylose broth, showed ‘daughter’ colonies on xylose agar, indicating that in even the slowest xylose fermenters the xylose utilizing power is potentially retained as a latent characteristic.

On solid media the author found that all the strains of *B. typhosus* tested utilized both dulcitol and arabinose. In fluid media nearly half of the strains produced acid in dulcitol, while only a small number were able to develop acid from arabinose. All the strains gave ‘daughter’ colonies on rhamnose agar, but none produced acid in rhamnose broth. No ‘daughter’ colonies were seen on raffinose agar, and no acid was produced in rhamnose broth. The author is not in favour of applying the term ‘mutation’ to the changes described, as the bacteriologist is studying not only the morphology but also the biochemical reactions in thousands of generations. He prefers to employ the term ‘variants’ to the atypical varieties of bacteria. In a further part of his investigation he shows that, grown upon normal serum, typhoid bacteria do not become inagglutinable. On specific immune sera, they become inagglutinable at first, but eventually become agglutinable if the cultivation is persisted in for as long as 72 days. Inagglutinability of the typhoid bacillus is accompanied by inability to absorb agglutinin. No differences can be observed in these relations between the slow and the rapidly xylose-fermenting typhoid bacilli. The inagglutinable strains showed a changed reaction in regard to hydrogen-ion concentration of the environment as shown by acid agglutination tests. All the changes brought about by artificial environment in the typhoid bacillus were rapidly lost when the bacilli were returned to the usual cultural conditions. W. B.

Gratia, A. Studies on the d'Hérelle phenomenon. *J. Exper. M.*, 1921, **34**, 115.

Attention has already been directed (*Medical Science*, 1920, **2**, 182) to the fundamental experiments of d'Hérelle, who found that stools of patients recovering from bacillary dysentery contain a filterable substance which is capable of dissolving cultures of *B. shigae,* and that a few drops of the dissolved culture reproduces the same phenomena upon addition to another culture, a fact which d'Hérelle explained on the assumption that the dissolving or lytic agent is living, or as he called it, a ‘bacteriophage’. Kabeshima disputed this contention and maintained that the ‘bacteriophage’ is merely a catalyzer secreted by the leucocytes of the infected bowel, and is capable of activating a lytic proferment which he believed to exist in the body substance of the micro-organism. The subject was carried considerably farther by the observations of Bordet and Ciuca (vide *Medical Science,* 1921, **4**, 62). They injected guinea-pigs intraperitoneally with cultures of *B. coli*, and one day after the third inoculation the peritoneal exudate was found to have bacteriophagic properties in d'Hérelle's sense. They, however, made the remarkable observation that a culture of *B. coli* once dissolved by the peritoneal exudate and then filtered is able either to dissolve a second culture of *B. coli* or to inhibit its growth in broth. Neither the lysis nor the inhibition is however complete, since some of the bacteria always resist. Such bacilli are distinguished by the striking characteristic not only that they resist the lysis but that they themselves have acquired the lytic property and are capable of inducing lysis in a culture of normal *B. coli.* Further, when inoculated on sloped agar, they show mucoid, sticky colonies; they are less susceptible to phagocytosis and are more virulent than ordinary cultures. Most remarkable of all, these acquired properties are preserved even after passage through animals. This '*modified B. coli*' is believed by Bordet and Ciuca to be a variation arising under the influence of the peritoneal exudate and showing itself by an ability to secrete a lysin which dissolves the homologous bacteria. They regarded the phenomenon as a transmissible microbic autolytic property.

The present author, Gratia, has published a number of short communications on this subject, and they are here presented in a more complete form. He shows that the inhibition of growth by the lytic agent is greatly influenced by the reaction of the medium, being faint in a slightly acid (P_H 6·8) or neutral (P_H 7) or even slightly alkaline broth (P_H 7·4), but much more pronounced in a more alkaline medium (P_H 8 or 8·5). In a highly alkaline broth the inhibition is so marked that growth of the resistant bacterial individuals only begins after 36 to 48 hours. When spread on an agar slope of a young culture of *B. coli* the lytic agent clears the culture leaving only a few of the more resistant forms of *B. coli* which have survived the lysogenic process. Gratia succeeded in isolating, from a subculture of the original strain, a colony which was very sensitive to lysis, so that he was able to study the resistant (R) and the sensitive (S) strains side by side. Type S was found to grow quickly in artificial media and to be non-motile, whereas type R grew more slowly, was highly motile, much less susceptible to phagocytosis, and at the same time more virulent. Both types produced indole and fermented carbohydrates with the exception of saccharose. Both types were found to preserve their individuality after passage through guinea-pigs. In spite of showing a general degree of sensitivity to lysis the culture S was never completely dissolved. In other words, it was not homogeneous, but was composed of individuals with variable lysis-resisting properties, although only a few were so resistant as to survive contact with the undiluted lytic agent. On the other hand, only a few of the sensitive bacteria were so sensitive as to be dissolved by very dilute solutions of the lytic agent, a view which explains the fact that when diluted lytic agent is spread on an agar plate inoculated with *B. coli* its action is limited only to certain places considered by d'Hérelle to be 'colonies of bacteriophage'. The same clear areas are also observed when lysis-resisting cultures are subjected to the action of undiluted lysis agent. The lytic filtrate was specific in the sense that it was active on *B. coli* used in injecting the guinea-pig, but inactive on other strains of the same bacterium. By allowing the original lytic principle to act on cultures of the two types S and R two new filtrates were obtained. The first resulting from dissolution of the sensitive strain S was, like the original filtrate, specific. The second, which had been in contact with the resistant strain, was found by Martha Wollstein to have, in addition to its action on R strains, a marked effect on *B. dysenteriae* Shiga, *B. dysenteriae* Flexner, and *B. dysenteriae* Hiss, and a strain of *B. coli* which was not attacked by the original filtrate. By a series of successive passages through appropriate strains Gratia himself, in consequence of Miss Wollstein's observation, was able to extend the lytic power to other species, such as *B. typhosus*, *B. paratyphosus* A and B. W. B.

Lepper, Elizabeth H. The production of coliform infection in the urinary tract of rabbits. *J. Path. & Bacteriol.*, 1921, **24**, 192.

The authoress undertook a series of experiments to produce lesions in the kidney by intravenous injections of organism of the colon group in order to examine the inflammatory changes produced soon after infection, and to devise a method by which renal changes might be induced with a reasonable degree of certainty. Rabbits were the animals employed, and the effects of various strains in varying doses were studied with or without the intervention of complications such as obstruction of the ureter. When coliform bacilli appeared in the urine after intravenous injection of these microbes evidence of renal complications were found except in one case. Complete obstruction of a ureter for fifteen minutes suffices to make the kidney vulnerable to coliform organisms circulating in the blood. Severe perirenal infections do not readily spread to the kidney itself, but if a blood infection results from the infected focus a renal lesion may follow. W. B.

Seligmann, E. Die Diphtherie in Berlin. Eine seuchengeschichtliche Untersuchung. [**Diphtheria in Berlin; a study in the history of epidemics.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **92**, 171.

In this research the author has traced the history of diphtheria in Berlin from 1835 to the present time, and illustrates with figures and curves the course of the modern epidemic wave which began to appear in the fifties and reached its maximum about 1883. Extensive tables are given dealing with absolute and relative mortality as also the case mortality. The relation to seasons, age, sex, and other factors are carefully analysed. A special chapter is devoted to the manner in which the disease is spread and the means employed in the attempts to stamp it out. The relation of the decline of the epidemic to the employment of antitoxin is discussed in considerable detail. W. B.

Durand, P. Action des bacilles diphtériques sur les hydrates de carbone. [**Action of diphtheria bacillus on carbohydrates.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 982.

The author has tested the fermentation reactions of 224 strains of typical virulent diphtheria bacilli using Martin bouillon containing 1·5 per cent. of the respective carbohydrates tested. Litmus or brom-cresol purple were the indicators employed. Mannitol, dulcitol, sorbitol, xylose, mannose, lactose, starch inulin, and glycogen were never fermented. Glucose and laevulose were constantly and rapidly attacked. Glycerol, galactose, maltose, saccharose, and dextrin were variable.

The author's agglutination Type I fermented maltose and dextrin, but not glycerol, and galactose only slightly. Type II never fermented maltose, dextrin, or glycerol, but galactose and saccharose were intensely attacked. Types III, IV, and V fermented glycerol, galactose, maltose, and dextrin, but not saccharose. Sixty-three strains which did not fall into any of the five agglutination groups gave mostly the fermentation reactions of Types III, IV, and V, although five gave the fermentations of Type II.

W. B.

Durand, P., et **Guèrin, J.** De bacilles diphtériques et épidémiologie. [**Diphtheria bacilli and epidemiology.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 980.

Attention has already been directed (*Medical Science*, 1920, **2**, 485) to Durand's view that by agglutination and absorption tests diphtheria bacilli can be separated into five well-marked groups. In the present communication it is claimed that particular epidemics are due to the one and the same strain. In a series of small family epidemics the bacilli isolated were of the same type, from the different members, with one exception in which a brother and sister showed bacilli of Type V, whereas another brother showed a bacillus of Type IV. It may be remarked, however, that the last patient was in hospital six weeks before his type of bacillus was determined, and he may have had a superadded strain. In schools and hospitals the same kind of facts were elicited. In a particular boarding-school which had also day scholars there were four cases of diphtheria. All the scholars to the number of 125 were examined. Forty-five showed diphtheromorphic bacilli. In 29 these bacilli were isolated pure and were shown to comprise 7 of pseudo-diphtheria and 22 of true diphtheria. By the agglutination tests all the latter belonged to Type I. W. B.

Zurukzoglu, S. Zur Methodik der bakteriologischen Diphtheriediagnose. [**On the technique of the diphtheria diagnosis.**] *Centralbl. f. Bakteriol.* (&c.), 1921, Orig. **86**, 440.

In 1920 Klein recommended for diphtheria diagnosis the use of serum made uncoagulable by the addition of soda, the altered serum being then added to agar. In this way a transparent serum-agar was obtained. Wang (1918) recommended the use of a fluid ox-serum medium into which the infected swabs were placed and left to soak in the incubator overnight, a thick film being examined the following day. Zurukzoglu has tested the value of these two new methods in comparison with the old Loeffler-serum method. He finds that the Klein medium is so variable in composition, and at times the bacilli are so altered that it is of little value. With Wang's method 140 tests showed diphtheria bacilli in 44, whereas, with Loeffler's serum they were found in 48. Loeffler's serum in plates and in tubes was examined in 200 cases, and no difference was detected in the number of positive results. W. B.

Bachmann, W. Echte Diphtherie- und diphtherie-ähnliche Bazillen im Phagozytoseversuche. [**True diphtheria bacilli and pseudo-diphtheria bacilli in phagocytosis tests.**] *Centralbl. f. Bakteriol.* (&c.), 1921, Orig. **86**, 434.

The author examined a large number of cultures by Wright's opsonic technique to see whether it was possible to distinguish diphtheria from pseudo-diphtheria bacilli, and came to the conclusion that although true diphtheria bacilli in general seemed to be less easily phagocytosed than pseudo-diphtheria strains the method gave inconclusive results.

W. B.

Dernby, K. G., and **David, H.** **A study on the preparation of diphtheria toxin.** *J. Path. & Bacteriol.*, 1921, **24**, 150.

Although diphtheria toxin is prepared and used daily in immense quantities the optimal conditions for its preparation are not completely understood. Among recent workers, Bunker is of opinion that a highly important factor is the hydrogen-ion concentration of the medium, a view with which the present authors agree. They find that the diphtheria bacillus grows in a range of hydrogen-ion concentration from $P_H=6$ to $P_H=8\cdot3$, the optimum falling between $P_H=7\cdot2$ and $P_H=7\cdot6$. If sugar-free broth is used the reaction will shift towards the alkaline side during growth. The maximum production of toxin depends not only on the amount of growth but on the length of the time of incubation and the initial and final H-ion concentration. With eight days' incubation a medium with an initial P_H of 7·2 to 7·4 and a final P_H of 8·0 to 8·3 they obtained the best results. They describe a method of preparing a bouillon which they believe gives consistent results. W. B.

Spreitzer, O. H. Vergleichende Untersuchungen über neuere Färbemethoden für Tuberkelbazillen. [**A comparative estimate of some of the recent methods for staining tubercle bacilli.**] *Centralbl. f. Bakteriol.* (&c.), 1921, Orig. **86**, 458.

The author has tested comparatively on 360 specimens of sputa, five of the newer methods recommended for staining tubercle bacilli, viz. those of Joetten-Haarmann (1920), Schaedel (1919), Marx (1919), Ulrich (1919), and Konrich (1920). He finds that by all of them tubercle bacilli are demonstrated oftener than by the Ziehl-Neelsen method. He gives the preference, however, to that of Konrich which consists in staining with carbol-fuchsin, decolorization with a ten per cent. solution of sodium sulphite, and counterstaining with malachite green solution. W. B.

Bender, W. Zur Technik des Nachweises der Tuberkelbazillen in Sputum. [**Technique of demonstrating tubercle bacilli in sputum.**] *Centralbl. f. Bakteriol.* (&c.), 1921, Orig. **86**, 461.

In a comparative study of methods for staining tubercle bacilli the author has made a special study of that of Spengler, especially as modified by Tribondeau (1917). The author himself recommends another modification still, his technique being, hot carbol fuchsin for 2 min. decolorization in 3 per cent. acid (HCl) alcohol, and counterstaining in a 1 per cent. solution of picric acid for 1 min. In an examination of 1,012 sputa by his method the author found tubercle bacilli in 200. In the same series the results with Uhlenhuth's formalin method were found to be superior to those with the ordinary Ziehl-Neelsen technique. W. B.

McJunkin, F. A. Tuberculosis in guinea-pigs with an experimentally produced endothelial leukocytosis. *J. Med. Research*, 1921, **42**, 201.

During the week or two preceding the death of guinea-pigs infected with tubercle bacilli, the peripheral blood shows a considerable increase in large mononuclear leucocytes which the author regards as of endothelial origin. A similar change is met with after injections of *B. phlei, B. smegmatis,* and non-virulent cultures of *B. tuberculosis*. In order to determine the effect of the increase of these leucocytes on the course of tuberculosis, the author inoculated guinea-pigs with virulent T.B. and subsequently with non-infective acid-fast bacilli in sufficient dose to produce a leucocytosis. Both macroscopically and microscopically the animals that received injections of *B. phlei* and *B. smegmatis* differ from the controls living the same number of days in that the spleen is small, and that the necrosis of the leucocytic foci in its substance and in other organs is slight or absent. In all probability the guinea-pig offers little resistance to the growth of T.B. during the first ten to fourteen days of infection before the tuberculin test becomes positive, so that any beneficial effect from stimulation of the leucocyte which reacts to the greatest degree in tuberculosis would have to be initiated after this time. Injections of non-virulent cultures of *B. tuberculosis* appear to shorten somewhat the duration of the disease.

W. B.

Nègre, L., et **Boquet, A.** Recherches sur la valeur antigène des émulsions bacillaires et des extraits éthyliques et méthyliques de bacilles tuberculeux. [**Researches on the antigenic value of bacillary emulsions and ethylic and methylic extracts of tubercle bacilli.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 300.

The authors have studied the complement-fixing power of various tubercle antigens, and particularly recommend the use of extracts in methylic alcohol. Cultures six weeks old are sterilized at 120° C. for 30 minutes and are then filtered, the bacillary mass being washed with water and then dried. It is then treated with acetone for 24 hours, 1 c.cm. of acetone being used for 1 cgm. of bacilli. After extraction the bacilli are dried anew and are finally macerated for 10 to 12 days at 37° C. in methylic alcohol 99 per cent. The liquid separated by filtration constitutes the antigen recommended, and it is stated to be highly specific, at the same time very sensitive and also very durable. W. B.

Besredka, A. Culture des bacilles tuberculeux dans du jaune d'œuf. [**Culture of tubercle bacilli in the yolk of the egg.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 291.

Besredka recommends the use of the yolk of the egg for growing tubercle bacilli. The yolks of 20 eggs are added to 1 litre of distilled water which should be neutral. If the water is acid it must be carefully neutralized beforehand. The yolks in water are then clarified by means of soda 1 per cent., an operation which must be cautiously carried out. No other ingredient is added to the medium, which is sterilized at 110° C. for 15 minutes. At the end of four days the culture is at its optimum for the preparation of antigen for fixation tests, although growth takes place up to two months. W. B.

Rieux, J., et **Bass, Mlle.** Réaction de fixation (antigène de Besredka) et tuberculose. [**Fixation tests with Besredka's antigen, and tuberculosis.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 378.

Using Besredka's tubercle antigen the authors have examined the sera of 425 persons. Of these 78 were suffering from pulmonary tuberculosis, 6 from peritoneal tubercle, 28 from sero-fibrinous pleurisy, 44 from symptoms indicating enlargement of the tracheo-bronchial glands, 80 from supposed latent tuberculosis. The remaining 189 cases were not regarded as tuberculous. With the exception of one negative reaction all the cases of proved phthisis, gave positive reactions. The negative case was a combination of syphilis and tuberculosis and died of a rapidly caseating phthisis. In three cases a positive fixation was found before the demonstration of T.B. In the six cases of peritoneal tubercle a positive reaction was obtained four times. Of the two negative cases one died of tuberculous meningitis, the other left the hospital in a state of profound cachexia. Of the 28 cases of pleurisy 16 (57 per cent.) were positive, while of 44 cases of suspected enlargement of the tracheo-bronchial glands 20 (44 per cent.) were positive. The number of positive reactions given by 80 cases of suspected latent tubercle was 51 (63·75 per cent.). Among 148 cases of diseases of different kinds and in which there was no suspicion of tubercle there were 17 positive reactions (11·5 per cent.) and 131 negative (87·5 per cent.). The authors attribute the high degree of specificity to the complement-fixation technique with Besredka's antigen. W. B.

Fried, B., et **Moser, M.** Réaction de fixation à l'antigène de Besredka dans la tuberculose externe. [**Complement fixation with Besredka's reaction in surgical tuberculoses.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 388.

After a description of the exact technique employed, the authors give an analysis of 869 cases in which they have carried out the test. The age of the patients varied from 2 to 14 years. The series consisted of 196 cases of Pott's disease, 143 of *morbus coxae*, 116 of white swelling of knee, 158 osteo-articular lesions of the elbow, wrist, shoulder, and ankle, 56 of external tuberculous and 44 of enlarged glands. Included in the series were 24 cases of syphilis of bones and glands, 32 of non-tuberculous osteo-arthritis, and 100 cases of rickets. An analysis is given, of the negative and positive cases, from which the authors conclude that with rare exceptions a positive reaction permits the conclusion that there is an active tuberculous lesion. A negative reaction, however, does not exclude tubercle. The proportion of positive reactions in the early stages of surgical tuberculoses is high, but as they progress to cicatrization there is a considerable number of negative reactions. W. B.

Urbain, A., et **Fried, B.** De la spécificité de l'antigène tuberculeux de Besredka. [**On the specificity of Besredka's tubercle antigen.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 294.

This is a short paper dealing with the specificity of Besredka's tubercle antigen in complement-fixation tests. The first experiments deal with the behaviour of various non-tuberculous antigens in the presence of tuberculous sera, the second series with the action of various non-tuberculous sera on the antigen of Besredka. Non-tuberculous sera, such as the various anti-sera from horses inoculated with different bacteria, when brought into contact with tubercle antigen, do not fix complement, the only exception being antidiphtheritic sera. The sera of human beings suffering from enteric fever, erysipelas, nephritis, and osteomyelitis also give a negative reaction. Of 21 cases of diphtheria 5 gave a positive reaction which was attributed to the fact that each had been treated with diphtheria antitoxin. On the other hand antituberculous serum from the horse fixes complement in the presence of Besredka's antigen while the same serum was negative in the presence of non-tuberculous antigens. Human tuberculous serum acted similarly, except that in three cases out of 20 examined there was some fixation with diphtheria bacilli, and in two cases out of 15 with *B. subtilis*. The antigen of Besredka was regarded as possessing a relatively high degree of specificity. W. B.

BIOCHEMISTRY

Schneider, E. C., and Truesdell, D. A study of the influence of various circulatory conditions on the reaction to the low oxygen of rebreathing. *Am. J. Physiol.*, 1921, **56**, 241.

For the purpose of ascertaining, in connexion with selections for flying, whether certain conditions of the circulation may influence the ability for compensation to low oxygen pressure, ten special groups were selected from 2,000 cases. These groups included men with high and low systolic pressures and diastolic pressures, large and small pulse pressures, rapid and slow pulse-rates, and men in whom the systolic pressure showed a fall or a rise respectively when standing.

All of the groups responded in a similar manner and compensated to equally low pressures of oxygen. None of the conditions placed the heart or the nervous system under a handicap greater than is present in average conditions of the several circulatory factors considered. W. C.

Whipple, G. H., and collaborators (**Arnold, M. R., Carrier, E. B., Lee, F. W., Smith, H. P.**). **Blood-volume studies, Nos. V, VI, and VII.** *Am. J. Physiol.*, 1921, **56**, 313, 328, 336.

The estimation of the blood-volume by different methods has given results which show considerable discrepancies. Thus the blood-volume of dogs has been found to be 10 per cent. of body-weight by the dye methods, 8 per cent. by the CO method, and 7 per cent. by the Welcker method. In this series of investigations these discrepancies are accounted for as follows: The dye methods give a reasonably accurate estimation of the plasma volume: in dogs 4·8 per cent., i. e. 4·8 c.cm. of plasma for 100 gm. body-weight. The total haemoglobin is accurately estimated by either the CO method or the Welcker method and found as 4·2 per cent. of body-weight. This, therefore, indicates the red blood cell volume. In the past only one or the other has been estimated, and the total blood-volume has then been calculated on the assumption that the total plasma volume and total blood-cell volume bear to each other the same relation as is found in a centrifugalized sample of blood drawn from any of the usual sources. Thus, with a haematocrit reading of 50, the figures obtained would simply be doubled. This assumption is incorrect. The ratio of cells to plasma is not constant in all parts of the circulation. In arterioles and capillaries there is an excess of plasma over red cells.

In order to obtain the correct blood-volume it is necessary therefore to determine the plasma volume by a dye method and the red cell volume by the CO method or the Welcker method. The sum of these to which the authors add 0·2 c.cm. per 100 gm. body-weight as the volume of leucocytes gives the correct blood-volume. Thus, in dogs, 4·8 c.cm. plasma volume + 4·2 c.cm. red cell volume + 0·2 c.cm. white cell volume = 9·2 c.cm. is the correct value for the blood-volume per 100 gm. body-weight. Details of the various methods are given. W. C.

Wiechmann, E. Über die Durchlässigkeit der menschlichen roten Blutkörperchen für Anionen. [**The permeability of the human red blood corpuscles for anions.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 109.

In blood, whether hirudinized, citrated, or defibrinated, the ratio of Cl content of corpuscles and plasma (or serum) is 1 : 2·1, and this ratio tends to be maintained when corpuscles are suspended in isotonic NaCl solution; also when suspended in isotonic Na_2SO_4 there is a removal of Cl from the corpuscles. Under what are called uniform conditions—after 30 minutes bubbling of O_2 through the blood, and 2 hours stay of the corpuscular suspension in the ice-chest—human corpuscles show different permeability to different anions, as judged by the concentration of anion in corpuscle and menstruum: for SO_4'' 1 : 19·7 (very variable), PO_4''' 1 : 9·7 and for Br' 1 : 3·1. These relations apply both to citrated and to defibrinated blood. The permeability to PO_4''' is improved by rise of temperature and that for Br' is lessened by Ca ions. Various dyestuff anions were not taken up by the corpuscles. C. L. E.

Tisdall, F. F., Kramer, B., and **Howland, J. The concentration of sodium and potassium as compared with that of calcium and magnesium in the serum of patients with active infantile tetany.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 252.

The sodium, potassium, calcium, and magnesium content of the serum of children suffering from infantile tetany was examined.

The sodium content is within normal limits. The potassium is somewhat elevated, while the concentration of calcium is markedly diminished. Magnesium is normal. The $(Na + K)/(Ca + Mg)$ ratio in the normal infant is (average) 27·6, while in cases of infantile tetany = 44·5.

C. G. L. W.

Reimann, S. P., and **Sauter, M. D. Comparison of the blood and lymph bicarbonate after intravenous injection of sodium bicarbonate.** *J. Biol. Chem.*, 1921, **46**, 498.

When sodium bicarbonate is injected into the veins of dogs it distributes itself very rapidly between the blood and the lymph. This seems to show that the content of the lymph in alkali enters as a considerable factor into the question of the alkaline reserve. R. A. P.

Denis, W., and **Sisson, W. R. A study of the chlorine content of milk and blood after the ingestion of sodium chloride.** *J. Biol. Chem.*, 1921, **46**, 483.

Owing to some observations upon human subjects of the effect of diet upon the Cl concentration of the milk, some experiments were done upon goats. It was found that neither feeding upon a salt-free diet nor ingesting 1·2 gm. of sodium chloride per kilo of body-weight over a period of 6 days led to change in the chlorine concentration of the milk.

The effect of giving enough sodium chloride to increase the concentration in the blood-plasma led to increase in the amount of the salt in the milk with diminution in the volume of milk secreted. R. A. P.

Hastings, A. B., Murray, C. D., and Murray, H. A. Certain chemical changes in the blood after pyloric obstruction in dogs. *J. Biol. Chem.*, 1921, **46**, 223.

After closure of the pylorus in dogs the following effects were observed. There was a rise in the alkaline reserve of the blood, and a fall in the concentration of the Cl ions. These results confirm those of Macallum. The authors further found an increase in the concentration of calcium of the blood. The P_H of the plasma was not much affected. It is significant that all of these dogs developed some of the symptoms of tetany. There is a possibility that there is a causal connexion between the alkalosis and the tetany, though it is not considered that there is any real evidence of it.

R. A. P.

Mills, C. A. Chemical nature of tissue coagulins. The action of tissue extracts in the coagulation of blood. *J. Biol. Chem.*, 1921, **46**, 135.

There are at present several theories of coagulation extant. Of these, the theory known as that of Morawitz may be said to be the most generally established. Recent work by Dale and Walpole has led to a vindication of the essential correctness of the Morawitz theory. According to the latter, there is necessary for the coagulation of the blood, the interaction of prothrombin, calcium, and thrombokinase to form the clotting ferment, thrombin. This ferment acts upon the fibrinogen to form the clot, fibrin. All opposition to this clear picture of the features of coagulation has of course not died down completely. We have the view of Nolf, in which the process is regarded as due to the interaction of various colloids, as well as the views of Howell in which much prominence is given to the position of the antithrombin factors in the blood. Some workers, too, favour the older views of Wooldridge, which can be regarded to some extent as precursors of the Nolf views.

In the present papers by Mills, there is claimed to be a strong vindication of some of the work of Wooldridge. The latter had isolated a tissue fibrinogen which would accelerate the clotting of blood. This, he believed, to be a combination of lecithin with protein. He further believed that in the clot formed as the result of the action of this, some of the tissue fibrinogen actually took part. Mills has studied the effect of lung extracts upon the clotting of oxalated blood. He finds that they induce very rapid clotting. He has been able to demonstrate that the most rapid clotting is induced when he has present in his extract a compound of a phospholipin and a protein. The former corresponds to cephalin, and the latter to a globulin. The evidence upon which he bases his views is dependent upon selective extraction with various solvents, and also selective digestion. He shows, for instance, that the digestion of the compound with trypsin or with lipase respectively in each case lowers very considerably the activity possessed by the preparation in accelerating the clotting of the oxalated blood. The protein fraction seems to be quite specific to lung and kidney. It is not found in the liver and cannot be imitated by emulsions made with phospholipin and egg white. Further evidence in favour of the value of the union of phospholipin and protein in this connexion is obtained from the fact that the two substances when united show a much greater activity than when apart. He further claims that the fibrin formed by the use of this tissue fibrinogen has some of the latter in combination with it. This was a view also taken by Wooldridge.

In a study of the intravascular coagulation produced by the injection of lung extract into rabbits and dogs, he finds that the non-coagulability of the remaining fluid blood is due to an absence of fibrinogen, a view which has been taken by others. The negative phase blood induced by the injection of repeated small doses of lung extract, has the power of clotting oxalated blood more quickly. On his view this is due to the presence of extra tissue fibrinogen in it. (On the old view (Morawitz) it would be due to the presence of pre-formed thrombin.) It is interesting that he finds that this clotting accelerator is excreted in the urine. He has further found that the injection of acid into the blood of a dog, to the point of producing a fall in the alkaline reserve, is succeeded not by a negative phase of diminished coagulability but by a phase of increased coagulability.

The work is felt by the reviewer to be interesting. It is difficult to know, however, quite how we are to relate the phospholipin protein compound to the thrombokinase and the prothrombin of the Morawitz coagulation factors. Are we to believe that there is in the tissue a supply of fibrinogen or prothrombin as well as of thrombokinase? Or do these two factors both make up the thrombokinase? R. A. P.

Collip, J. B. The acid base exchange between the plasma and the red blood cells. *J. Biol. Chem.*, 1921, **46**, 61.

Confirmation is given of the recent work of Joffe and Poulton and others. There is found good evidence for a shift of the acid base equilibrium between corpuscles and plasma upon changing the CO_2 tension to which whole blood is exposed. It is further found that a solution of the ash of serum or of whole blood has a greater CO_2 combining capacity than that of the original serum or whole blood. This is taken to indicate that in the process of ashing there has been set free a certain amount of alkali, which was previously combined with protein. In this case the view that the protein acts as a weak acid competing with CO_2 for the base in the blood is supported.

The results are not in support of the views of Mellanby and Thomas. (For a discussion of the question see *Medical Science* 1920–1, **3**, 332.)

R. A. P.

Wilbrand, E. Schweissabsonderung und Blutzusammensetzung. [**Sweat excretion and blood composition.**] *Biochem. Ztschr.*, 1921, **118**, 61.

As the result of sitting in hot baths of the temperature of 50° C.–60° C., until a moderate degree of collapse was felt, the pulse being doubled in frequency, the following results have been obtained. In strong sweating there is a concentration of the blood, a decrease of 25 per cent. leading to collapse. The amount of water lost from the blood is greater, the greater the amount of the sweating. The tissues lose a corresponding amount of water. There is a loss also of protein and of NaCl from the serum which runs parallel to the degree of the sweating. The author has the view that the tissues hold to their NaCl closely, and that the first loss of this salt comes from the blood. R. A. P.

Teschendorf, W. Über die Gefässwirkung organischer Kationen und ihre Beeinflüssung durch unorganische Ionen. [**On the vasomotor effect of organic cations and their influence by inorganic ions.**] *Biochem. Ztschr.*, 1921, **118**, 267.

The effects of a number of vasoconstrictor substances upon the 'Trendelenburg' preparation of the frog's blood-vessels have been compared. The most powerful effect was produced by acetylcholine, dilutions of a milliard being effective for summer frogs.

Muscarin was much less effective and less so guanidin. Of the quaternary ammonium bases, tetramethylammonium chloride had a powerful effect upon the vessel, intermediate between that of acetylcholine and muscarin. Tetraethylammonium chloride was very like guanidin. Tetrapropylammonium chloride decreased the tonus of the blood-vessel. These effects can in general be inhibited by divalent inorganic cations. The effect of muscarin is reversed if the vessel preparation is perfused for long with barium chloride in low concentration. Muscarin and acetylcholine also show a reverse if the preparation is perfused for long with a small excess OH ions (alkali). R. A. P.

Weiss, C., and **Corson, A.** **Preliminary note on chemical changes in the blood of syphylitics under arsphenamin treatment.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 210.

Wechselmann some years ago emphasized the importance of studying the kidney efficiency of cases undergoing treatment with salvarsan, and ascribed most of the fatalities to renal defect, but since then no extensive work has been done in this field (see Elliott and Todd, *Archives Derm. & Syph.* 1920, **2**, 699, and Bailey and Mackay, *Arch. Int. Med.* 1920, **25**, 628). The authors have studied two cases of tertiary syphilis with optic atrophy which were treated with doses of 0·6 gm. of arsphenamine. During the treatment there was on occasion vomiting, diarrhoea, and pains in the legs. The injection caused a slight rise in non-protein nitrogen in the blood, and the blood-sugar was increased. In no case did the blood-sugar reach above the upper limits given as normal. C. G. L. W.

Voegtlin, C., and **Smith, H. W.** **Quantitative studies in chemotherapy. V. Intravenous versus intramuscular administration of arsphenamine. Curative power and minimum effective dose.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 357.

Clinical opinion has been divided as to the relative efficiency of the intravenous and intramuscular routes for the administration of the organic arsenic compounds in the treatment of trypanosome infections. The authors have attempted to get information on this matter by using a standard method of observing the time of relapse and the appearance of trypanosomes in the blood of rats after infection and treatment and of animals surviving or dying within a stated time with no trypanosomes in the blood. The infective agent used was *T. equiperdum.* Various preparations of the arsphenamine type were used.

The intramuscular method appears to have the advantage in the lessened sudden toxic effects found in intravenous injections. The curative power by the two routes is about the same. The local irritant effect may be diminished by the use of neoarsphenamine, and it is possible that by the use of a new preparation this may still be decreased. The relation of the minimum lethal dose to the minimum effective dose is a substantial index to the curative power of a given drug under experimental conditions.

C. G. L. W.

Bornstein, A., and **Vogel, R.** Die Wirkung des Pilocarpins auf die Blutzusammensetzung. [**The effect of pilocarpine upon the composition of the blood.**] *Biochem. Ztschr.*, 1921, **118**, 1.

Working with dogs it has been shown that injections of pilocarpine cause the following alterations: an increase of haemoglobin content, an increase in the number of red blood corpuscles per c.cm., and an increase of the protein content. This change is claimed to be in the main due to the loss of water from the blood to the body tissues, and only in small part to the water losses in the sweat and excretions. In both rabbits and dogs, pilocarpine causes a hyperglycaemia. The effects are not altered by removal of the spleen, but they are antagonized by atropine. R. A. P.

Kraft, A., and **Leitch, N. M.** **The action of drugs in infection. I. The influence of morphine in experimental septicaemia.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 377.

Rabbits were treated with doses of morphine sulphate and then infected with a strain of streptococci from a case of human septicaemia. The injection of morphine lowers the resistance of the animals to infection. This is probably due to inhibition of phagocytosis, increase in intestinal stasis, with increased production of toxins and a general depression of the body temperature, of metabolism, and the body defence.

C. G. L. W.

Friedberg, E. Quantitative Messung der zeitlichen Kaffeinausscheidung beim Menschen nach einer biologischen Methode. [**Quantitative estimation of the rate of caffeine excretion in the human subject by the use of a biological method.**] *Biochem. Ztschr.*, 1921, **118**, 164.

The biological method used was the reaction of isolated muscle fibres from a frog's sartorius to concentrations of caffeine. Observation of the effects were made microscopically. It is claimed that the method gives exact results. The following are some of the main conclusions. 0·00007 gm. of caffeine can be detected by the method. The amount of caffeine excreted in individual portions of urine is dependent upon the amount of the urine. The kidneys can split off caffeine in very small concentrations. The diuretic effect is only in part dependent upon the dose given. It also depends upon the probable concentration in the blood and the water content of the organism. In hydraemia the diuretic effect of small doses is excessive. 10 mgm. is the smallest amount of orally-administered caffeine to produce noticeable excretion in the urine. Small doses of coffee show excretion in the urine. Caffeine is also detectable in the urine after the smoking of caffeine-containing tobacco. In all the experiments the velocity of excretion is rapid. R. A. P.

Hofvendahl, A. Die Bekampfung der Cocainvergiftung im Tierversuch. [**The antidotes to cocaine poisoning in animal experiments.**] *Biochem. Ztschr.*, 1921, **117**, 55.

Attention was directed to the question of antidotes to cocaine poisoning by the case of a child of 10 years old. This child had been poisoned through the nose with a 10 per cent. cocaine solution. The symptoms of the case were a strong motor excitation accompanied by pupil dilatation, pulse very frequent, and numbness. In the hope of counteracting the effect of the cocaine with a substance which stimulated the parasympathetic the author injected 0·01 gm. of pilocarpine. His idea was to compensate the cocaine effect and also to produce a rapid sweating and diuresis which would be likely to remove the poison rapidly. The result was apparently very rapid. In a few minutes the patient became visibly quieter, and in 10 minutes became conscious.

A repetition of the procedure upon dogs was not followed with any success. It appeared that the conditions of sweating, &c., were not quite comparable. Further, it was not found possible to combat the symptoms of cocaine poisoning in dogs by the use of amyl nitrate and physiological saline. The effects of cocaine poisoning observed in dogs were convulsions, of a tonic nature at first, but gradually shading off into clonic and then tetanic fits in one of which the animal died. The fits are produced, according to the work of Feinberg and Blumenthal, by stimulation of the cerebrum. This led to the trial of the effect of sleeping drugs, such as chloral hydrate, veronal, and scopolamine hydrobromide. Veronal proved to be the best drug for the purpose. Its effect was produced best when given so that its action was rapid, i.e. intravenously. The doses required to produce the results in dogs and cats are given. R. A. P.

Murlin, J. R. Results of nutritional surveys in U.S. training camps. *Tr. Coll. Phys., Phila.*, 1919, **41**, 149. (*Chem. Abstr.*, 1921, **15**, 1337.)

The winter ration of U. S. troops in France contained over 5,000 cal. per man daily. In the army, the total daily consumption of food per man averaged 3,633 cals. Each man requires approximately 400 more cals. during the period October to March than during the remainder of the year. The caloric intake at mess bore no relation to the additional caloric intake at the canteen. The number of articles of food used in the mess of private soldiers in a training camp ranged from 50–55, and decreased to about 15 in the field; the officers' messes showed a much greater variety; the number used in civilian families is about 39. Very strict mess discipline was not inconsistent with good physical results, one regiment showing an average gain of 6·6 lb. per man in 5 months' training. C. G. L. W.

Sure, B. Amino-acids in nutrition. Is proline a growth-limiting factor in the proteins of peas (*Vicia sativa*)? What nucleus in zein is responsible for supplementing these proteins. *J. Biol. Chem.*, 1921, **46**, 443.

It appears from this paper that it is possible that our knowledge of the indispensable amino-acids required by the body for growth may not yet be complete. The investigation here was directed to the question as to why zein, the protein from maize, is able to supplement the deficiencies of a diet in which pea protein constitutes the protein source. Zein contains no tryptophane or lysine. From the results of the experimental addition of various amino-acids to the pea protein diet, it is claimed that the deficiency is not due to the amino-acids amanine, leucine, valine, tryptophane, lysine, cystine, tyrosine, or proline. As zein further contains very little arginine or histidine it is suggested that there is some unknown amino-acid responsible.

R. A. P.

McCollum, E. V., Simmonds, N., and **Parsons, H. T. Supplementary protein values in foods. 1. The nutritive properties of animal tissues. 2. Supplementary dietary relations between animal tissues and cereal and legume seeds. 3. The supplementary dietary relations between the proteins of the cereal grains and the potato. 4. The supplementary relations of cereal grain with cereal grain; legume seed with legume seed; and cereal grain with legume seed with respect to improvement in the quality of their proteins. 5. Supplementary relations of the proteins of milk for those of cereals and of milk for those of legume seeds.** *J. Biol. Chem.*, 1921, **47**, 111.

In this extensive work the authors are attempting to solve problems of malnutrition from the widest standpoint. They draw attention to the importance of slight errors of nutrition which, though not serious enough to constitute real disease, such as beri-beri or scurvy, nevertheless play an extensive part in the resistance of individuals to disease, and to the effects of diminished vitality. In the course of their paper, they refer in illustration to some information communicated by Stefansson. Previous to 1850, it appears that dental caries was absent or very rare in Iceland. At this time the diet of the inhabitants consisted of milk, mutton, fish, fowl, the eggs of wild birds. The only vegetable food eaten regularly was carrageen moss, though potatoes and turnips were to a certain extent eaten. Since 1850, cases of dental caries have become gradually more common, and infected teeth are now found in large numbers. The deterioration of the teeth apparently began at a time when cereals and sugar were regularly imported into Iceland as food. Similar observations seem to have been made in the case of the Eskimo. On the whole the advance of civilization, with its increasing urban life, have led to the greater reliance upon cereal foods in the diets to such an extent that the result may be disastrous unless the adequate dietary corrections are properly understood.

In order to detect fine shades of difference involved in malnutrition of different grades of severity, rats have been closely observed in their habits throughout life. Signs of senility, fertility, and power of rearing successfully two or three generations of young upon experimental diets, are all used to indicate condition. A case of slight malnutrition, for instance, may not show up until the animal in question has to support the extra burden of producing milk or bearing young. It has been found that even a slight want of harmony in all the constituents of a complete diet may exercise a definite influence upon vitality when using the tests employed. As an illustration of the type of result obtained, the following may be quoted:

Lot 1405 was fed upon	peas	72·5	per cent.
	potatoes	25·0	„
	NaCl	1·0	„
	$CaCO_3$	1·5	„

Lot 2172 upon	peas	31·8	per cent.
	potatoes	25·0	„
	NaCl	1·0	„
	CaCO$_3$	1·5	„
	casein	10·0	„
	dextrin	30·7	„
And lot 1459 upon	peas	62·5	per cent.
	potatoes	25·0	„
	casein	10·0	„
	NaCl	1·0	„
	CaCO$_3$	1·5	„

Lot 1405 did not produce young; in 1459 young were produced but not reared successfully; lot 2172 reared two generations of young. Diet 1405 contained more fat soluble A than either of the others, the absence of casein made it inferior. Lot 2172 contained less protein and phosphorus actually than 1405, yet the quality of the diet was superior. To quote the authors' words: 'They represent a type of diet in which a small variation of quality upward in one or another factor, as protein or salts, may so modify the early history of the experimental animals as to make a particular factor, e. g. fat soluble A content, appear in one set of results to be adequate for physiological needs of the animals, while a variation in the quality downward either in protein or salts, such variation at the same time being well within physiological limits, may entirely change the deductions with respect to the value of the constant factor fat soluble A.' The case illustrates the success of the method of attacking this type of problem. It is only by careful study of all the factors concerned which show the fallacy of deductions such as those recently made by Hess and Unger, in which they concluded erroneously that the fat soluble A factor is not of importance in the nutrition of the human infant.

Summarizing the general conclusions, it was found that kidney, liver, and muscle proteins of the ox, as protein sources, possess about the same value as the wheat kernel. The first limiting factor in their use is calcium content, and the second sodium chloride. Liver and kidney, in addition, contain an abundance of fat soluble A, and of water soluble B, and (when fresh and raw) of water soluble C. They are remarkably efficient as supplements to the cereal proteins, though more so to wheat than to maize. They do not supplement the mineral deficiencies of cereals, or legume seeds, nor as proteins do they supplement legume seeds as well as they do cereals. The nitrogenous compounds of the potato improve slightly the biological value of the proteins of cereal and legume seeds, though not so effectively as kidney, muscle, liver, and milk. Not much is gained by an attempt to improve the value of a given cereal or legume protein with another of the same class.

The several foods are arranged in order of the biological value of their proteins, beef kidney being the best.

Beef kidney, Wheat	Milk Liver (beef)	Muscle (round steak) Barley Rye	Maize Oats	Soy beans Navy beans Pea

Milk is a particularly valuable article of diet, because even though it is not so good at correcting the deficiencies of seed and tuber diets as animal tissue proteins, it is a supplement in respect to other factors such as calcium and fat soluble A. R. A. P.

O'Reilly, L., and **McCabe, E. H.** **The available carbohydrate in thrice-boiled vegetables.** *J. Biol. Chem.*, 1921, **46**, 83.

The data in this paper were obtained in connexion with the use of thrice-cooked vegetables in the treatment of diabetics. It was found that the use of 20 parts of water for each boiling practically freed from carbohydrate, vegetable marrow, lettuce, and celery. Canned spinach, canned asparagus, turnips, beets, and onions could be made almost carbohydrate free. Cauliflower, cabbage, carrots, pumpkin, and canned string beans, even after this treatment, retained 0·5 per cent. of their available carbohydrate. The addition of about 0·1 per cent. sodium bicarbonate usually favoured the extraction of the carbohydrate. R. A. P.

Palmer, L. S., and **Kennedy, C.** **The relation of the plant carotinoids to the growth and reproduction of albino rats.** *J. Biol. Chem.*, 1921, **46**, 559.

The available data in the literature upon the suggested identity between the fat soluble vitamine and the carotinoid pigment of the plant are carefully reviewed in this paper. The conclusion reached from the literature is that there is no strong evidence for an identity of the two substances. There are further added the results of some fresh experiments, all of which lead to the conclusion that the vitamine and the carotinoid pigments are not identical. First, no trace of carotinoid pigment could be found in a thorough examination of the tissues of albino rats. Secondly, a ration made from ewes' milk giving good results for growth and reproduction with rats contained only 0·000013 per cent. of carotin. Thirdly, carotinoid-free egg-yolk was used with success in a diet as the sole source of fat soluble vitamine. In addition a comparison between the value of various substances as sources of fat soluble vitamine and their content of carotin showed the widest divergence in the distribution of the two substances.

It appears, therefore, from the above that the difference between these two substances is scientifically established. R. A. P.

Thannhauser, S. J., and **Schaber, H.** Experimentelle Studien über den Nucleinstoffwechsel (xiii). Zur Frage der intermediären Urikolyse beim Menschen. [**Experimental studies on nuclein metabolism (xiii). On intermediary uricolysis in the human subject.**] *Ztschr. f. physiol. Chem.*, 1921, **115**, 170.

Experiments in support of the authors' view that uric acid is the end product of purine metabolism in the human subject. Five individuals with healthy kidneys were injected with guanosin and with adenosin. In four cases practically quantitative excretion of uric acid followed. In the fifth case only about half of the theoretical amount of uric acid appeared in the urine after injection of adenosin and still less after guanosin, and even uric acid itself, injected as the sodium salt, was recovered only to the extent of 62 per cent. It transpired that this abnormal individual came from a family afflicted with gout, so that this result may have some significance.

H. W. D.

Elias, H., und **Sammartino, U.** Ueber die Rolle der Säure im Kohlenhydratstoffwechsel. 4. Die Beziehungen von Säure und Alkali zur Adrenalinglykosurie. [**On the rôle of acid in carbohydrate metabolism. 4. The relation of acid and alkali to adrenalin glycosuria.**] *Biochem. Ztschr.*, 1921, **117**, 10.

The paper gives a lengthy history of the subject in question. The author finds that glycosuria produced by the injection of acids into rabbits is not accompanied with constriction of the vessels in the liver, it differs, therefore, from adrenalin glycosuria in this respect. The increased amount of acid in the blood after the injection of adrenalin, which persists as long as three hours after the injection, is found to be due to lactic acid in part. The lactic acid content of the liver may be raised as much as three times its normal amount. A study of the sugar mobilizing effect produced by adrenalin in the perfused liver of the tortoise brought out the result that alkali stopped the effect of the adrenalin. This was apparently not due to destruction of the adrenalin because neutralization of the alkaline perfusion fluid containing adrenalin restored the active property. It is concluded that acid has an adjuvant effect to adrenalin in connexion with sugar mobilization. The reader is referred in this connexion to the abstract of the paper of Langfeldt.
R. A. P.

Eisenhardt, W., und **Schaefer, R.** Schwankungen im Chloridstoffwechsel unter dem Einfluss der menstruellen Vorgänge. [**Changes in the chloride metabolism under the influence of the menstrual changes.**] *Biochem. Ztschr.*, 1921, **118**, 34.

The chlorides in the blood undergo changes during the menstrual period. One or two days before the beginning or at the actual beginning of the menses, there is found a relative hyperchloraemia, and in most cases an absolute one. The chloride changes disappear at the end of the menstrual period. The authors think that the changes are in some way concerned with the blood loss, though in two cases they noticed such changes as an accompaniment of amenorrhoea. One of these cases apparently had an attack of nose bleeding at the beginning of the amenorrhoeal period. R. A. P.

Harris, J. A., and **Benedict, F. G.** **The variation and the statistical constants of basal metabolism in man.** *J. Biol. Chem.*, 1921, **46**, 257.

The basal metabolism represents the minimal amount of energy required by the body when surrounded by a temperature of about 30° C., and when fasting and in complete repose. It has been somewhat difficult to assess what is the best standard of comparison. The question of the best way of obtaining the constant for such a comparison is discussed, with the help of statistical methods. It is found that in general the metabolism of an individual shows wider variations from the mean according to the duration of the period of time over which the observations have been distributed. It appears, therefore, that the metabolism of the normal subject is, to a certain extent, in a state of flux. Several tables dealing with the statistics of the question are given. R. A. P.

Blunt, K., and **Dye, M.** **Basal metabolism of normal women.** *J. Biol. Chem.*, 1921, **47**, 69.

This laborious research comprised some 216 observations upon women's metabolism under various conditions. It is unfortunate that the object for which it was initiated, namely, to find out whether there was any periodic variation at the menstrual period, should have been without fruit. They could observe no definite change in the basal metabolism during menstruation. It is noteworthy that the daily variation for the individual, as found by Benedict, is quite considerable. This shows the danger of drawing conclusions based upon too few observations of the normal. R. A. P.

Moore, L. M. **Experimental studies on the regulation of body temperature, Nos. IV and V.** *Am. J. Physiol.*, 1921, **56**, 365.

The author had previously shown that an increase in intracranial pressure brought about by mechanical means is followed by a rise in temperature in rabbits. Since Weed and McKibben had found that intravenous injections of hypotonic salt solutions increased the cerebrospinal pressure in cats and hypertonic solutions diminished it, the effect of the injection of such solution on the temperature was studied in rabbits. All solutions, even the isotonic salt solution, gave a rise in temperature. The strongest hypertonic salt solution, however, gave a preliminary fall. Nevertheless, the author believes that these results confirm her view of a correlation between cerebrospinal pressure and body temperature. (Note by Abstractor: The fallacy which arises from the fact that water which has been allowed to stand gets contaminated with bacterial products having a pyrogenetic action has apparently not been considered in these experiments. It would explain all the results recorded in this paper.) W. C.

RADIOLOGY

Radiodiagnosis.

Wels, P. Untermehungen zur Diagnose und zum Entetechungs mechanismus des idiopathischen Zwerchfellhochstandes. [**Investigation on the diagnosis and mode of production of idiopathic undue curvature of the diaphragm.**] [**B.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 162.

The author distinguishes between this condition and eventratio diaphragmatica, by which name formerly it was generally known, and insists that the method of pneumo-peritoneum in cases of undue curvature obscures the picture. He considers that the distension of stomach and of transverse colon found in these cases is secondary to the muscular defect and not causal thereof: nevertheless a vicious circle arises and the gastro-intestinal condition tends to stabilize that of the diaphragm. Similarly he believes that the small volume of the lung met with in these cases is secondary and due to diminution of the normal space available for pulmonary growth, and that a primary pulmonary atrophy from the disuse with secondary undue curvature of the diaphragm is not the true explanation of the condition. W. S. L.-B.

Lazeanu. Revue critique sur la détermination du volume du coeur par les méthodes radiologiques. [**A critical revue on the determination of the volume of the heart by radiological methods.**] [**B.**] *J. de radiol. et d'électrol.*, 1921, **5**, 219.

The author states that the various cardiac affections reveal themselves by modifications in the shape or volume of the heart; these can be brought into evidence more accurately by radiology than by clinical examination. The deformations given by simple radiography are corrected by orthoradiography or by tele-radiography; the former is preferred by most radiologists. As regards the various diameters it is stated that increase of the longitudinal diameter points to hypertrophy of the left ventricle, increase of the horizontal diameter to hypertrophy of the right heart, and increase of the basal diameter to hypertrophy of the ventricles at their bases. The recent work of Vaquez and Bordet is then referred to, in which other diameters are also considered, and authors who have elaborated various other points are also mentioned.

Lazeanu then compares his own observations with those previously made by Vaquez and Bordet, and confirms them. P. L.-B.

Jaulin et **Limouzi.** Utilité de la recherche radiographique des lesions osseuses dans les sciatiques. [**The use of radiographic research on osseous lesions in sciatica.**] [**B.**] *Arch. d'électric. méd.*, 1921, **29**, 172.

The authors point out that sciatica so-called is in many cases secondary to some other lesion, such as Pott's disease of the spine, carcinoma of the spine, &c., and that therefore, radiographic examination may be of great use in these cases. They give the chief signs pointing to a vertebral lesion which indicate X-ray examination of the lumbo-sacral region and those indicating an X-ray examination of the region of the hip. It is also pointed out that in some cases there is no pain although there be a marked lesion of the lumbo-sacral region. A short account of the authors' routine method of examination is given, and the paper is completed by giving the observations on nine cases. P. L.-B.

Boquet et **de Beaujeu, J.** Ectopie de la rate cause d'erreur de radiologie gastrique. [**Ectopia of the spleen: a cause of error in radiology of the stomach.**] *Arch. d'électric. méd.*, 1921, **29**, 134.

The authors enumerate various causes which may give rise to error in radiography of the stomach; they may be intrinsic or extrinsic. They record a curious and rare cause which led to a wrong diagnosis, namely, ectopia of the spleen. The patient was a woman of forty who had suffered from gastric disturbances for some years; recently the pain and indigestion had been worse and accompanied by irregular vomiting 4–5 hours after a meal. Clinical examination revealed nothing beyond a furred tongue and enlarged abdomen with splashing. X-ray examination showed an enlarged and dilated stomach; on the greater curvature was a small notch seen in the left lateral position lying down; it remained after the stomach was empty. The diagnosis made was a neoplasm of the greater curvature. At operation the stomach was large and atonic, no tumour was found, nor ulcer, the larger curvature appeared normal. On turning up the transverse colon it was found to be fastened down on the left side; it passed under a pedicle containing large veins; this was followed until the spleen was reached in the true pelvis. The pedicle was twisted on itself two and a half times. The spleen was enlarged, the posterior surface of the stomach was normal. Splenectomy was performed. The spleen by its traction must have caused the deformity of the stomach; later on examination could not reveal the absence of the spleen. The authors think that a pneumo-peritoneum alone would have given any aid to diagnosis. P. L.-B.

Massart. Les fractures du fémur méconnus chez l'enfant rachitique. [**Unrecognized fractures of the femur in rickety children.**] *J. de méd. et chir. prat.*, 1921, January, p. 9. (*Arch. d'électric. méd.*, 1921, **29**, 91.)

Ignorance of the lesion, the difficulty of deciding as to the uselessness of the injured member, because of the youth of the patient, and absence of the usual clinical signs of fracture, are the reasons why these lesions remain unrecognized. Often they are only discovered later because of the calcareous mass formed on consolidation; they are frequently found in cases of children with rickets. In recent lesions, the clinical symptoms are somewhat vague; injury is at a minimum, since functional impotence is lacking with a child who does not walk; there is neither ecchymosis, nor crepitus, nor abnormal mobility. In old cases, chance discovery of a calcareous mass and varus becoming more accentuated every day, point to diagnosis. Thus, systematic radiographic examination, employed at the least sign, can alone give certain diagnosis, and it will show, in recent cases, either diaphysial fractures, complete or incomplete, according to the varied images of osseous fissures, and sometimes difficult to discover, or fractures close to an epiphysis involving especially the lower epiphysis, and giving very clear images. In old cases, radiography will only confirm, though completing, the diagnosis furnished by a calcareous mass, deformity and angularity of the thigh. It will also be of use, as in other fractures, in conducting and supervising the treatment.
S. U. L.-B.

Radiotherapy.

Murphy, J. B., Witherbee, W. D., Craig, S. L., Hussey, R. G., Sturm, E. Effect of small doses of X-rays on hypertrophied tonsils and other lymphoid structures of the nasopharynx. *J. Exper. M.*, 1921, **33**, 815.

Extending their work upon the effects of X-rays upon lymphoid tissue, the authors have employed irradiation in the treatment of hypertrophied tonsils and adenoids. In the past treatment in this way has been by use of large doses, so that it has approached the danger-point for the patient. The authors' work has shown that extensive reduction of lymphoid tissue can be induced by small doses of X-rays well within the safety limit, and they have now applied the method to 46 patients ranging in age from 3½ to 45 years and observed one month or longer after treatment. The method has been to irradiate a region about three inches square beneath the angle of the jaw on each side, occasionally with irradiation of the back of the neck just below the posterior occipital region when the amount of adenoid tissue was excessive. The spark-gap was eight inches between points, current 5 ma., ten inches distance from the target to the highest point of skin exposed.

filtration 3 mm. aluminium and time varying from 3 to 7 minutes according to the age of the individual. Recently fractional doses (four or more at two-week intervals and lasting 3 min. 18 sec.) have been recommended. The tonsils themselves were definitely enlarged and frequently showed plugging of the crypts with exudate. Usually a definite diminution in size was noted after a single exposure and the mouths of the crypts became patent, thus permitting escape of the contained exudation. No patients were treated when the throat showed signs of acute inflammation. Short histories of eleven typical cases are given and a table indicating the results in the entire series of 46. Photographs are also included of drawings made during progress of some of the cases. W. S. L.-B.

Groedel, F. M. The disappearance of a goitre and improvement of cardiac insufficiency by irradiation of the ovaries. *Strahlentherapie*, 1920, April, p. 1047. (*J. de radiol. et d'électrol.*, 1921, **5**, 42.)

The existence of a correlation between the various endocrine glands and of an interdependence of their functions on activity has been discussed many times. In particular it has been tried to establish a connexion between the function of the ovaries and that of the thyroid.

Graf also mentioned the appearance of an exophthalmic goitre following hysterectomy in one case and following destruction of the ovaries by radiotherapy in another.

On the other hand Mannaberg observed excellent results in ten patients suffering from Graves's disease and treated by radiotherapy by Kienböck, and Salzmann has published more recently (1919) an observation on a patient treated by radiotherapy for a fibroid in which a goitre of the size of two fists seemed to diminish very rapidly after existing 15 years, and the tachycardia and diarrhoea to disappear.

It seems then that cessation of the ovarian activity might react on the function of the thyroid, more often as a moderator than an incentive, and that this point has not been discussed.

Groedel's observation argues along the same lines. A patient examined and treated by him in 1908 for 'cardiac insufficiency', with a goitre about the size of two fists, suffered in 1912 with such severe metrorrhagia and anaemia that hysterectomy (it was a question of a small fibroid) was judged impossible and radiotherapy advised. Carried out by Groedel with complete success the menopause resulted in three series of sittings repeated after two months (the patient was 45 years old), at the same time that the goitre although large disappeared almost completely, and also all the cardiac symptoms.

This 'action at a distance' of the radiotherapy should be taken into consideration and would justify perhaps an attempt at systematic destruction of the ovaries by radiotherapy in the case of patients suffering from exophthalmic goitre and approaching the climacteric.

Analogous attempts seemed equally justified before deciding upon surgical intervention, often dangerous, for the removal of large goitres. They would be the more interesting, seeing that in true goitre direct radiotherapy is generally followed by small enough results. P. L.-B.

KJAERGAARD, S. Carcinoma efter Rœntgenbehandling af Knæledstuberkulose. [**Carcinoma following X-ray treatment for tuberculosis of the knee.**] *Hosp.-Tid.*, 1921, **64**, 32–8.

Kjærgaard's patient was a woman, aged 22, who, at the age of 4, developed tuberculosis of the left knee with fistulae as a sequel to an injury. At the age of 12 and for the next five years she was given intermittent ambulant treatment with the X-rays. There was no record of X-ray dermatitis. At the age of 19 she fell, tearing the soft tissues immediately above the patella and exposing the femur. The granulating wound would not heal, and some time later an exploratory excision revealed typical epithelioma. Amputation was refused till she was practically moribund. At the necropsy amyloid disease was found, as well as extensive tuberculosis of the lungs and intestines, but there were no malignant metastases, not even in the lymphatic glands in the neighbourhood of the epithelioma. Commenting on this sequel: X-ray treatment—atrophy of the skin—trauma—ulceration—carcinoma, Kjærgaard suggests that there is a certain risk of the same sequence for the many patients whose X-ray treatment has left them with areas of atrophic skin. C. L.

BÉCLÈRE. La radiothérapie dans la maladie de Basedow. [**Radiotherapy in Graves's disease.**] *J. méd. franç.*, 1920, **9**, 302. (*J. de radiol. et d'électrol.*, 1921, **5**, 137.)

The author takes for his guide cardiac disorders as indicated by the frequency and instability of the pulse. Each morning, while the patient is lying on his back, the pulse is taken, then, the patient immediately assuming a vertical position, it is counted again. Thus two pulse-curves are obtained. As treatment proceeds, these two curves, at first very elevated and distant from each other, become progressively lower and nearer; when the pulse in the recumbent position is not more than 80, the author either suspends the irradiations or gives them considerably less frequently. The patient gains weight and subjective symptoms are less numerous. A ray is used whose power of penetration, measured by means of the spintherometer, corresponds to a spark equivalent to 20 cm.; it is filtered through 5 mm. of aluminium, and the distance of the anticathode from the skin is 20 cm. A localizing cylinder of lead glass 10 cm. in diameter, serves to limit the radiations. At the first séance the two lateral regions of the neck are successively irradiated; at the second séance the anterior part of the neck and the upper part of the sternal region are treated, and the following séances are alternate repetitions of these two positions. The author prefers moderate doses at short intervals; weekly séances without more than three hours for each irradiation. Treatment should have for its object the function and not the lesion, and should be guided by disorders of the circulation and action of the pulse. All reaction of the skin must be avoided and care must be taken not to produce deficient thyroid secretion.

S. U. L.-B.

Radiotechnique.

Warnekros. Radiography in the third stage of labour. *Arch. f. Gynaek.*, 1918, p. 266. (*J. de radiol. et d'électrol.*, 1921, **5**, 232.)

By injecting a sterile opaque liquid into the umbilical vein immediately after the birth of the child, the author renders the placenta opaque. He uses barium sulphate and allows the blood to escape at first, so as to avoid a pressure which would rupture the vessels. Usually the placenta is separated from the edge. With very few exceptions it passes with one edge in front and thus reaches the vagina, and it is only here that the inversion is produced which causes the foetal surface to appear at the vulva. In some radiographs the separation is seen to begin at the centre. Separation begins at the moment that the uterus retracts, immediately after the expulsion of the foetus; in all the radiographs taken in the first five minutes after the birth of the child, the placenta had separated completely. Only on one occasion has the author been able to photograph the placenta in its normal position attached to the internal wall; it was a case of twins; injection and radiography were carried out before the birth of the second child, whose presence undoubtedly hindered uterine retraction. This fact proves that it is not the injection which brings about immediate separation.

P. L.-B.

Guthmann, H. Über den Gehalt der Röntgenzimmerluft an Ozon und salpetriger Säure und über die Ursache der Röntgengasvergiftung (Ozonwirkung). [**On the ozone and nitrous acid contained in the air of the X-ray room and on the causes of the symptoms produced by such air.**] *Strahlentherapie*, 1921, **12**, 262.

The symptoms associated with X-radiation are partially due to contamination of the air in X-ray rooms. The two principal substances concerned are nitrous acid and ozone. Quantitative estimations were made of the amounts of these bodies present in the air of the unventilated X-ray room both before and after running the apparatus and the findings for nitrous acid compared with those obtained from similar observations upon ordinary air and the air of chemical laboratories.

From these experiments it appeared that the amount of nitrous acid present in ordinary air showed a constant value which differed only slightly from that obtained from the air of X-ray rooms, while in chemical laboratories nitrous acid was present in amounts up to ten times as much as that found in the worst X-ray room. Nevertheless laboratory workers exhibited no suggestion of symptoms resembling those of 'Röntgen gas' intoxication, whereas X-ray workers frequently showed inflammatory or irritable conditions of the respiratory tract. Hence the conclusion may be drawn that nitrous acid is certainly not present in the air of the X-ray room in such amount as to produce any ill effect upon either patient or operator. A point of interest brought out in the investigation was that where high tension apparatus was in a different room from the X-ray tubes, the leads being carried from one room to the other through glass in the dividing wall, higher nitrous acid values were consistently obtained for the apparatus room than for the raying room. Incidentally it was also shown that the resistance of an enclosed spark-gap is for practical purposes impossible of calculation, and depends to a great extent upon temperature, moisture, the amount of the oxides of nitrogen produced, and the length of time for which the apparatus is working.

In dealing with the question of the ozone content of X-ray room air the amount theoretically possible was first determined by laboratory methods and calculation and then estimations were made of the amount actually present. Experiment showed that an increase of 23 per cent. in the potential of the field between two high tension wires increased the amount of ozone produced by 50 per cent. The quantitative estimation of ozone actually present in the X-ray room is very difficult, as all nitrous acid must first be removed, and the amount of ozone generated depends upon numerous factors such as the height of the potential gradient in air, the moisture present, and ionization of the air by direct, scattered, and secondary radiation. The figure calculated from experiment is, however, never reached, owing to the spontaneous formation of oxygen from part of the ozone produced. Konrich has shown conclusively that a proportion of 0·5 mgm. ozone per c.cm. of air must not be exceeded, or such ill effects as irritable cough, exhaustion, blood changes, &c., will be brought about. Comparing this with the results of the ozone estimations made, it appears that under unfavourable conditions ozone is produced in the X-ray room in amounts which may be as much as seven times as large as Konrich's figure. Herein lies the toxicity of air in X-ray rooms.

The results of these investigations have a practical bearing upon the construction of X-ray apparatus. The high tension circuit must be reduced to a minimum, must have as smooth a surface as possible, and be free from angles, points, and bends. By these means the formation of ozone can be restricted. Of next importance is the replacing of the parallel gap by a voltmeter, and the use of a gas-filled series gap to avoid the production of nitrous acid.

The conclusions drawn are that the phenomena commonly appearing in X-ray workers, of chronic blood-changes, exhaustion, and fatigue, bear a great resemblance to the symptoms of ozone poisoning, but may be ameliorated or avoided by proper planning of apparatus, adequate ventilation, and good personal hygiene. The correctness of the findings is supported by the following points: (1) the difference between the symptoms of chronic nitrous acid poisoning and those of 'Röntgen gas' poisoning, and the close agreement between those of ozone poisoning and the latter; (2) the immensely greater amount of nitrous acid present in laboratory air than in the X-ray room without the occurrence in workers of any symptom resembling 'Röntgen gas' poisoning; (3) the occurrence of these symptoms in those working with apparatus without a parallel gap and having gas-filled series gaps.

Detailed results of the various experiments are given, and the apparatus used described. E. M. W.

Chaoul, H. Le rassembleur de rayons. Méthode pour l'abaissement du temps de pose en radiothérapie profonde. [**The ray collector. A method for decreasing the length of exposure in deep therapy.**] *München. med. Wchnschr.*, 1920, **67**, 861. (*J. de radiol. et d'électrol.*, 1921, **5**, 136.)

The apparatus is one for receiving the rays, except those of the cone directly utilized, on a thick paraffin envelope where secondary rays are produced whose action is added to that of the primary rays. Under a paraffin cylinder which surrounds the tube is arranged a sort of localizer of the same substance, in the shape of a truncated quadrangular pyramid. In this way an increased intensity of 60 per cent. and a reduction of 38 per cent. in the duration of the séance is effected. S. U. L.-B.

Radium Technique

Loisel, P. Recherche des corps radioactifs dans les eaux minérales. [**An investigation of the radioactive substances occurring in mineral springs.**] *J. de radiol. et d'électrol.*, 1920, **4**, 247.

Most mineral waters, especially those from deep springs, contain radioactive substances to which certain of their therapeutic properties are attributed. It is therefore important to determine the presence in such water of the various radioactive bodies, especially those—radium, thorium X, and actinium X—which give rise to emanations.

A simple and satisfactory method of estimating the activity of the radioactive material present consists in precipitating the material in the water and then investigating the activity of a thin uniform layer of the precipitate by means of an ionization chamber. Full details are given of the method of precipitation and the preparation of disks of the precipitate for the ionization chamber. The ionization current due to these disks is measured daily over a period of at least one month and the results plotted in the form of a curve, intensity against time in days.

Radium gives a curve falling rapidly at first, then rising more slowly, and reaching a maximum at the end of about thirty days. The variation is due to emanation occluded in the precipitate. Thorium X and actinium X give curves in the reverse direction. Both show an initial rise, the apex of the curve being reached at the end of 24 hours. The curve of actinium X then falls off the more slowly since the activity of this substance decreases by half in 11·4 days, while that of thorium X decreases by the same amount in 3·64 days. Curves are also shown for various mixtures of these bodies.

The method does not require costly laboratory apparatus, and the author claims that the results obtained are sufficiently precise to be useful to the medical hydrologist. E. M. W.

Radiobiology.

Lacassagne, A. Recherches expérimentales sur l'action des rayonnements β et γ du radium agissant dans les tissus par radiopuncture. [**Experimental research on the action of the β and γ rays of radium acting within the tissues by radiopuncture.**] *J. de radiol. et d'électrol.*, 1921, **5**, 160.

The author begins his paper by reviewing the early works on radium which led him to attempt to determine the relations existing between the degree of filtration of various parts, and the lesions, either caustic or selective, produced by radiations in certain normal tissues.

Experimental conditions. It was necessary to introduce into the interior of the organism a capsule capable of exercising simultaneously both its caustic action on a tissue of feeble radiosensibility and its selective action on elements of great radiosensibility. Then it had to be determined in what manner the nature and development of the lesions could be modified by varying the quantity and quality of the rays. A female rabbit was used in all cases; the capsule was introduced by puncture into the lumbar muscles on a level with the ovary. The muscle should show a caustic effect and the ovarian follicles a cytocaustic selective effect. The radioactive substance used was radium emanation in glass capillary tubes 1 mm. long and 0·5 mm. in external diameter. They were screened in various ways. The author describes the method by which the tube was introduced into the muscle. The animals were killed after various lengths of time. The area of necrosis was measured with compasses and complete transverse sections of the muscle removed for histological examination: the ovaries were weighed and fixed.

Modifications of striated muscle around the capsule and the development of the lesions. The author gives a detailed account of the macroscopic appearances of the muscle both in longitudinal and transverse section; from these it is seen that the area of degeneration has the shape of a regular cylinder with rounded ends. An account of the microscopical appearances follows; the general structure of the striated muscle fibres is preserved, but the tissue has undergone a complete necrosis with the disappearance of all detail, the cytoplasm becoming homogeneous and undergoing granular degeneration and disintegration of the nuclei, many of which have disappeared completely. It is a case of rapid and total tissue death due to a caustic action of the rays. At the external edge of the zone of degeneration the tissues appear normal, the change being abrupt; outside, the capillaries are dilated and in places extravasated red corpuscles fill the interfascicular spaces. Farther away the muscle is absolutely normal. Diffuse necrosis starts early; at times it can be distinguished by the naked eye forty hours after irradiation. Round the whitened area is a region of congestion. Microscopically the lesions are progressive from the periphery to the centre.

After 30 days the cylinder of necrosis is as clear and characteristic as after 12 days, but the congestion and oedema have disappeared. After 2½ months it is still visible, but the transverse diameter has decreased considerably. Histologically the necrosed muscle fibres tend to break up; the débris takes up the basic stain. The necrotic tissue is always surrounded by connective tissue in which are many giant cells. After 4½ months the lesion is much reduced in size and appears as a white line in the midst of fibrous tissue.

The influence of the quality of the irradiation on the extent of the diffuse radionecrosis. To determine this the following factors were varied: (1) the dose, (2) the time, (3) the thickness of the filter, (4) the metal used for filtration. As regards the first two the intensity, that is the dose divided by the time, was made to vary. The author only takes count of the mean intensity of the first 24 hours, calculated by dividing the amount of emanation destroyed during the first day by 24. The experiment showed that the diffuse necrosis increased with the intensity of irradiation up to a certain limit, after which it remained constant. As regards the total dose received it appeared that the caustic action produces its effect quickly in the first few hours of irradiation so that the diameter of the lesion does not increase with the dose received. Prolongation of the irradiation by the same tube of emanation does not appreciably increase the extent of the necrosis. To determine the influence of altering the thickness of the filter the extent of the lesions produced were observed when tubes of the same initial value screened with different thicknesses of platinum were used. A graph is given of the results of these experiments; from this it is seen: (1) that the extent of the lesion increases with the initial value of the tube, whatever be the thickness of the filter; (2) that the thinner the filter, the weaker the initial dose which produces necrosis; (3) that the greatest extent of necrosis is about the same whatever the filtration used, i. e. 7 mm. from the seat of irradiation.

The selective cytocaustic action of irradiation on the ovary. On the whole the lesions produced are similar to those produced by X-rays, but less pronounced and not absolutely identical in character. In the above experiments the chief characteristics were: (1) the selective action of the rays; (2) the lesions were proportional to the dose received; (3) the lesions were independent of the degree of filtration.

Which are the caustic and which the selective rays in irradiation by radium? The author gives no answer to this question. He says that there are many stages between hard and soft rays, but their separation can only be obtained by means of very strong filters and that in practice the rays used are not homogeneous.

The application to radium therapy. In the treatment of cancer in particular it should be decided whether selective rays alone should be used or whether caustic rays should also be added. In the former case the neoplastic cells are destroyed without injuring the normal tissues, whereas in the latter every living cell is destroyed. The production of a large focus of necrosis has certain dangers which are enumerated. In conclusion, the author states that although his arguments may reduce the use of radiation in cancer cases, they allow the following conclusions to be brought forward: (1) that radium puncture with filtered needles should be preferred to the use of unshielded tubes; (2) that the initial value of a capsule should not be greater than that indicated in the paper, otherwise damage would be done to the surrounding tissues; (3) that while the limit must not be passed beyond which necrosis of the tissues will be produced, sufficient intensity must be used to destroy the tumour; (4) that in applications on the surface or within cavities—in the case of tubes of great intensity—the secondary filter should be at least equal to the radius of the cylinder of necrosis.

P. L.-B.

Segale, G. G. L'action des rayons X et du radium sur les cartilages épiphysaires. [**The action of X-rays and of radium on the epiphyseal cartilages.**] *Radiol. med.*, 1920, **7**, 234. (*Arch. d'électric. méd.*, 1921, **29**, 92.)

In considering the possible effects of the rays on these tissues, the author puts forward five questions:

1. What modifications in development of the bone may result from variable conditions of treatment?
2. Can the development be arrested or retarded?
3. Are the lesions produced permanent and progressive, or transitory and susceptible of cure?

4. Is there a latent period, and, if so, what is it?

5. What histological modification is to be observed and how are the different cells affected?

The author's experiments were carried out on 41 white rats of different litters, all of them being between 8 and 14 days old. His conclusions are as follows:

1. Even when applied in a small dose, on a growing member, the rays stop development. This is more marked with γ- and β-rays of radium than with γ-rays alone.

2. The change begins rapidly, the latent period for a medium dose being less than four days.

3. Modifications are not transitory and do not tend to cure, they rather show a tendency to become aggravated and cause an early arrest of development.

4. When the shortening of the member begins to be noticeable, incurving and deformity of the bone may appear. There is thinning of the shaft and atrophy of the muscles.

5. A process of degeneration takes place in the cells and structural changes appear in their interior from five to eight days after a fairly strong dose. These changes are characteristic. There is no vascular modification.

Later, from 59 to 83 days after, when development has been partially arrested by the rays, a characteristic change in the structure and diminution of functional activity are evident. The β- and γ-rays of 20 mgm. of sulphate of radium, applied for one hour, produce, in two months, a particular condition, in which the cartilage is thickened but has lost its characteristic structure. There is always complete absence of vascularization and the osseous lamellae show modifications.

6. There is extreme radiosensibility of the epiphyseal cartilage in its active stage and there is very probably an alteration in the activity of the osteoblasts. S. U. L.-B.

MEDICAL SCIENCE

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

PNEUMONIA

Aetiology. Blühdorn states that **broncho-pneumonia in the new-born** may arise from : (1) aspiration (e.g. of milk) ; no matter how careful one may be this may occur ; (2) infection during birth ; and possibly (3) an infection may have occurred during intra-uterine life. This last must be very rare.

Clinical aspects. Any one who has examined a large number of cases of lobar pneumonia and of wounds of the chest realizes how difficult it is accurately to interpret the physical signs elicited on palpation, percussion, and auscultation, as so often they seem contradictory. We are much indebted to Zadek (1) for so thoroughly investigating 300 cases of unilateral lobar pneumonia, especially by recording changes in *vocal fremitus* and the breath sounds, and by determining the presence or absence of fluid in the pleural cavity. The important point is to try and explain weak or absent vocal fremitus over a consolidated lobe. Various possible explanations have been offered : (1) blocking of the larger bronchi with exudate, as in a 'massive pneumonia' ; (2) blocking of a large number of the smaller and smallest bronchi ; unfortunately both these phenomena are rare findings at autopsy ; (3) the great increase in volume of the consolidated lung causes it to press against the thoracic wall and it is prevented from vibrating. This may possibly hold true in cases of hepatization of an entire lung, but not so if only one lobe is consolidated ; (4) owing to the presence of an exudate into the pleural cavity, vocal fremitus is dampened or completely obliterated.

Zadek (1) included only cases of clear-cut lobar consolidation in his series of 300 unilateral pneumonias. The findings given in the extensive table are not his alone, but those of several physicians working together. There were equal numbers of men and of women amongst the patients and also some children. Unless at least 5 c.cm. of fluid were obtained on puncture an effusion was not diagnosed. The needling was done over the affected lobe on the 2nd to 7th day of disease. The depth of the layer of fluid was measured by thrusting the point against the lung, then withdrawing the needle and exhausting the syringe at the same time until the point came out of the parietal pleura and no more fluid was obtained. On the average, the fluid overlying the lung was about 1 cm. in depth. Amongst the 300 cases 54 died (18 per cent.), and autopsies were performed upon 51. At the post-mortem there was less than 5 c.cm. of fluid in 4 cases, 5 to 100 c.cm. on twelve occasions, 100 to 150 c.cm. in 25 cases, 150 to 250 c.cm. in 4 cases, and more than 250 c.cm. on six occasions. X-ray examinations had also been made, and it was found that, owing to consolidation of the lung, 50 to 250 c.cm. of fluid could not be detected by this means. On the other hand, this amount of fluid, in the absence of consolidation, may be made out by an X-ray.

Zadek (1) gives a very full table of the findings. The site of consolidation is noted, together with data as to increased or weakened vocal fremitus, and as to presence or absence of fluid. The character of the breath sounds is described under two headings, 'frank bronchial breathing', or 'absent or weakened bronchial breathing'. A close perusal of this table is necessary to bring out all the points of interest. A pleural exudate was present in 57 per cent. of the cases and decreased vocal fremitus in 66 per cent. How important a factor pleural exudate is in decreasing vocal fremitus is realized when it is seen that both were found together in 54·3 per cent. of all the cases. That the decreased vocal fremitus was not due to blocking of the bronchi follows from the fact that bronchial breathing was present in 142 out of 163 of this group of cases. In 2·7 per cent. of all the cases there was a pleural exudate together with increased vocal fremitus, but here there was massive infiltration of the whole lung. In only 11·7 per cent. of all cases could it be shown that weakening of vocal fremitus was due to blocking of the bronchi in a massively infiltrated lung.

In his 558 cases of lobar pneumonia Abrahams noted *herpes* in 95 (17 per cent.). Of these only 4 per cent. died, and the good prognosis of this sign again receives confirmation. Marked *delirium* was present in 22, or 4 per cent., of the cases. Three patients were admitted with acute mania. Defervescence occurred by *crisis* in 315 cases (56·4 per cent.). Five of these patients died subsequently, and 28 developed an empyema. In 113 instances the crisis was on the 7th day.

Foster has written a timely paper on *broncho-pneumonia.* After her work at a base hospital and elsewhere she is now convinced that this is a much more frequent disease than it is commonly thought to be, and that young adults, and not merely children and old people, are attacked. This fact was also borne in strongly upon the writer of this review during some time in France. It must be noted that Foster is not dealing with broncho-pneumonia in influenza. The physical signs may be very fleeting in character, and thus there may be marked differences between the findings at morning and evening examinations. The temperature chart may show but slight deviations from the normal and the pulse and respirations be but little raised.

In the confluent type involving a large part of one lobe the signs of consolidation may be so marked that he who runs may read. Or small patchy areas of dullness, with bronchial breathing and increased voice sounds may be found, and the diagnosis is plain. On other occasions, casual examination of the patient may reveal signs of a bronchitis only, but the strictest attention should be paid to slight differences in the quality of breath, spoken voice, and whispered voice sounds in adjacent areas not larger than those covered by the bell of the stethoscope. Even these slight changes from the normal cannot be fully understood unless we correlate with them the findings in similar cases *post mortem.* Only by doing this can we make our 'clinical' diagnosis coincide with our 'pathological' one. And this should be our aim. Even where no physical signs at all are made out, the X-ray picture may show small shadows—very often close to the hilum of the lung—or a peribronchial mottling suggestive of miliary tuberculosis. A later plate shows that these patches are fading away. So frequently was broncho-pneumonia found, that it was said in the hospital 'bronchitis is rarer than broncho-pneumonia'.

Type I pneumococcus may cause a broncho-pneumonia, but not so frequently as Type IV. Foster writes that 'probably a majority are caused by a streptococcus', but this is probably putting the case too strongly for that organism. The Americans had such sad experiences with streptococcal infections of the lungs following measles in the army camps that Foster emphasizes the need of isolating patients whose resistance is lowered by an acute infection. The attendant himself may be a menace to such a patient, for it has been shown that many healthy persons harbour haemolytic streptococci in their throats. Haemolytic streptococci often are the cause of an interstitial pneumonia characterized by infiltration and thickening of the structures about the bronchi and in the septa of the lungs. The infection extends along the lymphatics of the septa to the pleura, so that one of the earliest findings in such a case may be a purulent collection of fluid in the pleural cavity.

If the patient has not been seen in the acute stage of disease, a patch of slowly-resolving broncho-pneumonia at the apex of one lung may be mistaken for tuberculosis. According to Foster this diagnosis was often made even by tuberculosis specialists in the American army, but close observation over some length of time showed that the signs were clearing up.

Flandin and Debray report a case of *Friedländer's Bacillus pneumoniae* in a woman 40 years of age, who was taken ill suddenly with a chill, pain in the left side of the chest, and cough. She was admitted to hospital three days later. At this time her condition was serious: she was dyspnoeic and cyanosed and a low grade of icterus was present. She had a foetid rhinitis, the nostrils showed crusts of exudate, and there was a brownish discharge having a bad odour like that of ozoena. There was marked dullness over the left lower lobe, with decreased breath and voice sounds, but repeated puncture failed to find fluid. The fever decreased from the 5th to the 9th day by lysis, after which there were several slight elevations of temperature until the 13th day. Signs of frank consolidation with blowing breathing and subcrepitant râles did not appear until the 13th, and these continued up to the 20th day. The sputum was haemorrhagic, and on the 14th day Friedländer's bacillus was seen in great abundance in the sputum and grown in cultures. The authors consider that, as the foetid rhinitis was present from the first, the pneumonia and the jaundice were secondary to a septicaemia. The jaundice varied in degree on different days. The patient had completely recovered at the end of about a month.

Traumatic pneumonia. Pneumonia, as is well recognized, may follow contusion of the chest. Stern, in his book, *Ueber die traumatische Entstehung innerer Krankheiten*, distinguishes three classes of cases: (1) typical lobar pneumonia, (2) extensive haemorrhagic infiltration of the lung with an atypical course, and (3) broncho-pneumonia with circumscribed foci of infiltration. Lobar pneumonia may begin with a chill and rigor and rusty sputum, and may be accompanied by a high sustained fever, herpes labialis, and typical consolidation of one or more lobes. In the second class the temperature curve is more irregular and the signs of a generalized infection are not so marked. Very often there is typical rusty sputum, but it is very apt to contain more blood than in cases of lobar pneumonia. In the third class the consolidation is patchy, moist râles are heard, the condition of the patient is not so serious, and the prognosis is favourable.

Lichtschlag has analysed the findings of 211 autopsies performed during ten years at a large hospital in Breslau upon persons who were very severely contused. In 134 no lesions were found in the lungs. It could be said with certainty that in 54 of the remaining 77 cases the changes found in the lungs were not dependent upon the trauma, but had occurred before the accident, or had developed long after it. At the 23 remaining autopsies typical lobar pneumonia was found in 3 instances, broncho-pneumonia in 14, and in 6 cases haemorrhages under the pleura or in the lungs were found, but no pneumonia was present. Lichtschlag considers it very probable that, even without fracture of a rib, small haemorrhages into the lung occur. These may be absorbed without any pneumonia developing, or either lobar or broncho-pneumonia may set in. The injured lung constitutes a place of lowered resistance, where bacteria of the throat, or those brought by the blood-stream, may readily multiply and cause pneumonia.

Complications. There were 6 cases of *meningitis*, or 1 per cent., amongst the 558 cases of lobar pneumonia in the series of Abrahams. In 25 cases (4·5 per cent.) *meningism* was a feature, and lumbar puncture was performed, but merely clear fluid withdrawn. *Pericarditis* was discovered in 11 cases (2 per cent.), and of these 4, or 36 per cent., died. Infective *endocarditis* was diagnosed, or found *post mortem* in 4 cases, or 0·72 per cent. of the whole series. *Jaundice* was a prominent feature of 7 cases. *Arthritis* occurred in 2 cases and extensive *thrombosis* in one. *Nephritis* was present in 2 cases.

Abrahams noted 116 cases of *empyema* (20·8 per cent.). Only 30 of these required resection of a rib; the others were treated by repeated aspiration. The mortality amongst all the cases of empyema was 20 per cent.

Foster writes that empyema is a more frequent complication after broncho-pneumonia than after the lobar variety. The diagnosis may present great difficulty. A walled-off pleural abscess may be present for months without causing any marked diurnal variations in the temperature, but an increased pulse-rate is of great significance. The empyema is very often interlobar, and the needle, not the physical signs, shows its position. Foster has found that there may be a skodaic note in the adjacent lung. Sometimes she has noted that the pus lies beneath a point of acute tenderness in the chest wall. So often the lung is already bound down by adhesions that there is no displacement of the liver downward or of the heart towards the opposite side. Indeed, compensatory emphysema of the contralateral lung may displace the heart towards the affected side. This fact has been proven *post mortem*. Repeated aspiration of the infected fluid is the treatment of choice, and removal of a rib to secure drainage should be deferred as long as the patient continues to improve. If, in the end, this measure is necessary to get rid of thick pus, it will be found that by the formation of adhesions the infection has been walled off. It is of the utmost importance to remember that more than one pocket of pus may be present.

Lung abscess may follow broncho-pneumonia, and if no adhesions are present it is possible, by inducing artificial pneumothorax, to put the lung at rest and aid healing. If the lung cannot be collapsed in this way lobectomy has to be done.

Bouchut and Contamin describe a case of *pneumothorax* occurring in lobar pneumonia. The patient, a man aged 24, was admitted into hospital the day after a typical onset of pneumonia with pain in the left side, dyspnoea, and high fever. The left side of the chest was immobile, and the vesicular murmur and tactile fremitus were absent except at the apex, but there was no change in the percussion note. There was a *bruit d'airain*, amphoric breathing, and coin-sound below the angle of the scapula. The temperature remained high for five days and then fell by lysis. The signs of pneumothorax progressively diminished and cleared up on the 10th day. The sputum was typical of pneumonia, contained many pneumococci, and no tubercle bacilli were found. There was no history suggestive of old tubercle. X-rays showed a triangular mass of consolidation in the left lower lobe, and another plate, taken from another angle, revealed a localized pneumothorax between the base of the wedge of consolidation and the thoracic wall. There was some fluid at the base of the lung. A few c.cm. of lemon-coloured fluid were drawn off. No organisms were seen and none grew out on culture. Fifty-one per cent. of the cells in the exudate were polynuclear eosinophils.

Pneumothorax is not common in broncho-pneumonia and is very rare in the lobar variety. It is of interest that, although the pneumothorax was localized, the signs were much more widespread. The authors think that the pneumothorax was due to the rupture of an emphysematous vesicle close to an area of consolidation. The eosinophils suggested a favourable prognosis and that an empyema would not form.

Sequelae. As in the case of adults, Karger has found that in children also, following an attack of pneumonia, the X-ray picture of the affected lobe still shows a shadow for three or four weeks after the temperature has become normal. Nothing abnormal is made out by the ordinary methods of physical examination, so Karger holds that the shadow cannot be due to an exudate in the alveoli. Nor can it be caused by a thickening of the pleura, for absorption of such a plastic exudate would not be completed within a month. Even before physical signs reveal consolidation of the lung in a case of pneumonia, the X-ray detects a shadow which can only be due to a congestion of the blood-vessels of the lobe. Thus Karger concludes that the shadow after pneumonia is due to the same cause. Knowing the frequency with which an effusion of a small amount of fluid occurs during the course of a pneumonia, it does not seem to the reviewer that Karger is justified in ruling out a thin layer of liquid as the cause of the shadow.

Karger has also noticed that, after an attack of influenza during the recent pandemic, children often looked quite ill and were either pale or cyanosed, although temperature, pulse, and respirations were normal. On auscultation fine crepitations were heard—generally on both sides of the chest. These sounded as if they were produced very close to the bell of the stethoscope. On going into the histories carefully, Karger concluded that broncho-pneumonia had been present before he had seen the children, that the crepitations were pleural in origin, that they were of little consequence, and that no special treatment was required.

Zadek (2) notes that *post-pneumonic contralateral pleurisy* has not been described in recent German monographs on the lungs. He records two such cases seen amongst about 600 cases of croupous pneumonia. In both instances about three weeks after the fall of temperature and after resolution of the affected lobe was complete, or almost complete, and the patient was gaining in weight, there was pain in the chest on the side opposed to the original pneumonia. Fever was absent and there was no cough or expectoration.

On examination, signs of a small effusion were made out at the base and the X-ray confirmed this, but showed no foci of consolidation. The shadow of the fluid increased in extent and in each case a few c.cm. of fluid were withdrawn with a needle for examination. It was turbid, contained polynuclear leucocytes, but no organisms. In both cases the fluid was absorbed within a month's time. Zadek shows that in the absence of fever and sputum, and considering the interval following the fall of temperature, this pleurisy cannot be regarded as a manifestation of pneumonia in the lung on *this* side. The afebrile period and nature of the cells in the exudate are both evidence against the idea of a lighting up of an old tuberculosis. Zadek suggests that perhaps in the contralateral pleural cavity there had been localized a collection of pneumococci, which had got there from the blood-stream, and rejects the idea of a lymphatic connexion between the two pleural sacs.

Mortality. Abrahams has given an excellent account of 558 consecutive cases of lobar pneumonia seen in the Aldershot Command from April 1915 until October 1917. Amongst these soldiers there were only 61 deaths (10·9 per cent.): 23 with empyema, 6 with meningitis, 4 with pericarditis, and 4 with infective endocarditis. In some cases the last two lesions were combined. No complications were present in 28 of the men who died. In 115 cases of double pneumonia there were 33 deaths (28·7 per cent.).

Diagnosis. Blühdorn discusses the diagnosis of *broncho-pneumonia in the new-born*, which is such a fatal disease. The diagnosis is not difficult if there be fever, dyspnoea, and dilating alae nasi, cough, and cyanosis. Vomiting and diarrhoea are common. Often there is no fever, and generally no cough. Very frequently no signs of pneumonia can be made out on auscultation. Blühdorn considers that cyanosis and attacks of asphyxia are the most important signs. Given cyanosis, three conditions call for consideration: (1) broncho-pneumonia, (2) sepsis, with or without pneumonia, and (3) congenital heart disease. Cyanosis that is intermittent suggests broncho-pneumonia, especially if it is accompanied by asphyxial attacks. A permanent cyanosis of moderate degree makes one think of a septic infection. The cyanosis of congenital heart disease is permanent and often the child is almost black. If there are no attacks of asphyxia, morbus cordis is suggested. Cyanosis may be the only sign in congenital heart disease and no heart murmurs may be audible. Broncho-pneumonia is very apt to occur in premature infants, as the respiratory centre only gradually assumes its function. There is also a form of cyanosis which occurs in infants who are not getting sufficient nourishment and fluids. This disappears rapidly on giving fluids.

Prophylaxis. Southworth pleads for *segregation* of cases of pneumonia, especially amongst children. Many times he has seen pneumonia spread rapidly after the appearance of one case in a measles ward. It took a long time for us to learn to isolate cases of pulmonary tuberculosis, and Southworth looks forward to the time when cases of pneumonia will no longer be treated in a general ward. The rapidity with which pneumonia spread amongst patients who had influenza was proved on many occasions during the waves of the recent pandemic.

Treatment. Sloboziano has already written a paper on *intrapulmonary injections of antipneumococcus serum* in cases of broncho-pneumonia (*Presse méd.*, 1920, No. 70). He now describes certain of the effects caused in the untreated, as well as in the treated, lung. Quite often areas of congestion or haemorrhage result. These were also seen in 14 experimental dogs, of which 6 were normal and healthy before the injection. The animals weighed from 8 to 12 kilograms, approximately the weight of an infant of 8 to 24 months. From 8 to 12 c.cm. of Pasteur Institute antipneumococcus serum were injected through the thoracic wall into the lung. The lesions found at autopsy on two of the dogs are described, but similar results were noted in the other twelve animals. The dogs were killed by *piqûre* of the medulla, three hours and half an hour after the injection, respectively. Multiple infarcts were caused in the former and a marked congestion of the contralateral lung in the latter.

To prevent blood flowing from the pulmonary vessels into the bronchi, the trachea was tied before the lungs were removed from the body. On inspection of the lungs, many areas of congestion varying from the size of a pea to that of a two-shilling piece were seen, both in the injected lobe and also in the other lung. The centre of these was of a reddish-violet colour, outside this there was a zone of grey, and the outer parts were of a dark red. These foci were surrounded by a zone of congestion, broad or narrow according to the size of the lesion. These areas were firm, and that at the site of injection was about the size of a walnut. The lungs weighed 3 to 4 times their normal weight—even the lung not injected. On section, the congested areas were triangular in shape like infarcts, with their base towards the pleura. A portion of this mass did not float in water. The cut surface of the lung shared in the general congestion and in places haemorrhages into the lung parenchyma were seen. The bronchus leading to the 'infarct' was filled with clotted blood, and clots might be found in the lower part of the trachea and in some of the bronchi of both lungs, where more 'bronchial infarcts' (as Sloboziano is tempted to call them) had resulted. On microscopic examination, there was no thrombosis and no emboli in the vessels of these 'infarcts', but the bronchioles were filled with blood. At certain points there was great distension of the perivascular spaces, which were oedematous or filled with red blood cells. This lesion was observed even in the contralateral lung. The alveoli contained much blood and some desquamated epithelium; the capillaries of the alveolar walls were distended with blood or were ruptured.

Many of the lesions can be explained by the injury caused at the point of injection, where haemorrhage is bound to occur. The blood may flow into the bronchi and may even reach the trachea. Thus more 'bronchial infarcts' in the same lung and also in the one not injected are caused. Gravity is responsible for this extension of the lesions, but probably violent inspiratory efforts, or even coughing, may play some part.

But there are lesions of another class, which are not so easily explained. These may be found in either lung and were most frequent in the second dog described. In such cases the blood does not come by way of the bronchial tree, but the lesions probably represent reflex effects brought about by action of the sympathetic supply to the small vessels of the lung. Here the small bronchi contain no blood, but desquamated epithelial cells may be found in their lumina. The alveoli are filled with red cells and this phenomenon may be noted with the naked eye. Other air sacs may contain oedema fluid and desquamated epithelial cells. There is perivascular haemorrhage in these areas, which may in turn press on the vessels and almost obliterate the lumen. The adventitia of the small vessels may be injured and distorted by haemorrhage into its substance, and Sloboziano suggests that the filaments of the sympathetic may be injured and vasodilatation result. In support of this explanation of the changes found at a distance, Sloboziano cites Babinski's observation upon one effect of sympathetic injury. The latter has shown that if a hand, from which the arterial supply has been cut off by injury, be plunged into hot water, the opposite member shows marked vasodilatation.

Sloboziano utters a warning about the possible bad effects of injections made directly into the lungs.

Intravenous injections of a solution of *glucose* were used to a considerable extent in the United States in the treatment of pneumonia during the influenza epidemic. John gives his experience with this form of therapy, and at the same time draws certain general conclusions about the benefits which result, and discusses the physiological effects. He claims that: (1) glucose makes the patient more comfortable, (2) it induces sleep and rest, (3) elimination through the kidney and skin is increased, and (4) the heart action is slowed and the pulse volume is raised.

A chill quite often follows intravenous injections of glucose; after the first dose there may be none, but it may occur after any one of the subsequent doses. Briefly, one cannot predict when the patient will have a chill. All the glucose is used in the body and none is excreted by the urine when the equivalent of 200 to 300 calories is administered in twenty-four hours. This is not to be wondered at, as Woodyatt found that there was no glucose in the urine when he gave the equivalent of 6,000 calories in one day, i.e. 0·8 to 0·9 gm. per hour per kilogramme of body-weight. Not a single accident occurred in 1,200 administrations of glucose intravenously.

John found that if the glucose in concentrations of from 1 to 5 per cent. in distilled water was added to a suspension of red cells, haemolysis occurred, but with solutions above 5 per cent. concentration no haemolysis resulted. On the other hand, if normal saline was used, no haemolysis followed with strengths of from 1 to 20 per cent. of glucose, or even higher. As a routine, John employed 250 c.cm. of a 10 per cent. aqueous solution of chemically pure glucose twice or three times a day. In some instances a 30 per cent. solution was used to supply more fuel to the heart-muscle. It was sterilized by boiling or in the autoclave and kept on ice until used. The treatment should be commenced as soon as the diagnosis of pneumonia has been made, and the injections should be given slowly, allowing 15 to 25 minutes for the process. John gives 1 c.cm. of the tincture of digitalis, 8 mgm. of morphine sulphate, and 0·64 mgm. of atropine sulphate in the 250 c.cm. of glucose solution.

Artificial pneumothorax has proved a very valuable measure in the treatment of tuberculosis of the lungs for some years now. It has been used in cases of pleurisy with effusion, and in cases of dry pleurisy, in bronchiectasis, and in cases of pulmonary abscess. Friedemann, during the past two years, has employed artificial pneumothorax in the treatment of 9 cases of lobar pneumonia. He considers that the results have been favourable. All the patients recovered. A new chapter for Hilton's *Rest and Pain* could be written on this subject, for the relief of the stabbing pleuritic pain is apparently very striking as soon as enough gas is injected to separate the two layers of the inflamed membrane. Friedemann is also of the opinion that toxic symptoms rapidly decrease in severity, for, with lessened movement of the chest wall, flow in the lymphatics must be lessened.

As a rule, the temperature falls by lysis in the course of a few days. The author does not like to state positively that the disease is cut short by this treatment, but evidently he thinks so.

The object of the treatment is to place the affected lung at rest, and Friedemann injects from 400 to 600 c.cm. of nitrogen in the 5th intercostal space in the mid-axillary line. If the patient experiences great oppression the injection is immediately stopped. In one case, owing to extensive adhesions between the two layers of the pleura, only 50 c.cm. could be injected. Only cases of true lobar pneumonia should be treated in this way and only if the disease is confined to one lung. After the first treatment in 2 of the 9 cases, the disease spread to the opposite side, but no bad results followed. If crisis or lysis does not occur after two days have elapsed, the injection is repeated. Leschke's portable apparatus makes it possible to treat patients in their own homes. It remains to be seen whether this new form of treatment in pneumonias, accompanied by great pleuritic pain, is better than that of strapping the chest with adhesive plaster.

Brooks and Carroll state that there can be little doubt that in the majority of cases of pneumonia that end fatally it is a 'cardiac death'. An analysis of 5,000 post-mortem reports at an American army hospital in France showed this. The burden is thrown upon the right side of the heart; hence the dictum, 'always listen to the pulmonary second sound'. The reserve force of the right heart is small even in health. In pneumonia it is much decreased by: (1) the increase in the resistance to the pulmonary circulation, as shown very prettily by Gross's X-ray pictures of lungs in various stages of hepatization, where it is seen that the vessels cannot everywhere be injected; (2) in pneumonia parenchymatous degeneration of the heart-muscle results. But failure of the right heart may occur after but little warning, as the small reserve force is soon exhausted when it is called upon. Increased dullness to the right of the sternum, visible impulse of the right ventricle beneath the xiphoid cartilage, fullness of the veins of the neck, sudden increase in dyspnoea accompanied by substernal discomfort, all tell the tale of extra strain thrown upon the right side of the heart.

Brooks and Carroll emphasize once more the importance of absolute physical and mental rest for the patient, and this cannot be provided if unnecessary examining of the patient is carried out. They recommend the administration of *digitalis* as soon as the diagnosis has been made, so as to be ready later on if an extra call upon the strength of the heart has to be made. They give from 15 to 20 minims of the tincture every 2 or 3 hours until the slowing effect and a fuller pulse are obtained. The dose is then reduced to 5 minims every 3 hours. If necessary, a larger dose may be given later, and, if suddenly more is called for, they give digipuratum orally or intravenously. The digitalis should be tested upon animals before using. All this is not new, but early digitalizing of the heart should be given a more extensive trial. The writers state their good results in general terms only.

In *broncho-pneumonia of the new-born* it is most important, says Blühdorn, to give fluids both by mouth and by the rectum. He describes a method of producing and administering oxygen when a gas cylinder is not to hand. A flask is closed with a rubber cork through which two glass tubes (with glass funnels attached by rubber tubes) are inserted. One of the glass tubes dips down into a quantity of hydrogen peroxide, and through the funnel some potassium permanganate is poured and the rubber connecting tube clamped. The other glass tube does not reach the liquid, but the oxygen which is formed escapes through it when the tube is unclamped and allowed to flow out to the funnel placed over the child's face. Blühdorn recommends alcohol rubs for the child to support the circulation. Feeding is often a most difficult matter as the child's stomach is so frequently upset. In attacks of asphyxia artificial respiration must be resorted to.

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A. M.

MALARIA

Epidemiology. Glynn and Matthews report a fatal case, in a girl aged 17, of malignant tertian contracted in the north of England. The case is remarkable as being the first example recorded in recent years in England of indigenous malignant tertian malaria and of fatal indigenous malaria. Commenting on this case Blacklock comes to the conclusion that it was an acute primary attack, and that there was no evidence that infection was acquired by other means than a mosquito bite. The records of the incubation period and crescent formation render it probable that the girl was infected in a northern health resort, where anophelines are plentiful (*A. maculipennis*, *A. bifurcatus*, and *A. plumbeus*).

James states that during recent years the number of deaths in England registered as due to malaria contracted abroad has been usually between 50 and 60 per annum, but that in 1917 it rose to 126, in 1918 to 197, and in the first nine months of 1919 to 199, most of the deaths in 1918 and 1919 being among young men.

Brulé, May, and Lermoyez, who record a case of indigenous malignant tertian in a man aged 50, state that, though innumerable cases of indigenous benign tertian have occurred, only nine examples are on record in which the parasite of malignant tertian has been found in malaria contracted in France. In this number are included a mild case reported by Oettinger and Deguignand in a youth aged 18, who had spent his early life in Dordogne, a district free from marshes and where malaria is unknown, and a fatal case reported by Weil and Plichet. Both the cases had probably contracted the disease in Paris during the war.

Dupérié, who reports two cases of indigenous benign malaria in children at Bordeaux, points out that this town is particularly liable to the disease, soldiers repatriated from Salonica, foreign labourers engaged on the quays, and Spanish workmen forming a considerable contingent of carriers who only need a suitable anopheles to spread the infection.

Seyfarth had an opportuity of studying numerous cases of malaria at Gümurdshina, a small Turco-Bulgarian sea-coast town in Thrace, where the disease was so severe that from July 1–December 31, 1917, 187 deaths were certified as due to malaria. The character of the disease was quite different from that usually described, so that the Turkish, Bulgarian, and German medical officers often mistook it for typhoid fever. Dysenteriform varieties of tropical malaria were frequently observed. Tenderness and pain in the appendix area often led to the erroneous diagnosis of appendicitis. A mixed infection of malignant tertian and typhus was very frequent and attended with a high mortality.

Hoskin gives the following statistics of 500 cases of malaria examined consecutively at the Ministry of Pensions. 356 had contracted the disease on the Salonica front, 62 in Egypt and Palestine, 45 in East Africa, and 37 in other theatres of war, including a few recurrences of fever contracted during service in India prior to 1914. 69 or 16·4 per cent. had been discharged as permanently unfit, the highest percentage—28·9—of these discharges being among the cases contracted in East Africa. The average time spent in a malarial country before the soldier was transferred to a non-malarial theatre of war was considerably less in East Africa than that spent in Salonica and in Egypt and Palestine, probably owing to the length of the lines of communication, which was responsible for delay in bringing up supplies and establishing hospitals with adequate accommodation and necessary comforts.

Aetiology. According to Debuys, who records an illustrative case, the presence of carriers in a household is the probable explanation of the apparently unsuccessful treatment of those cases of malarial infection that do not respond to the proper use of quinine or of those that are proved to be cured, though the patients return with a supposed relapse which is in reality a reinfection. He records the case of a boy aged six years brought to hospital with the complaint of having had fever for two months. Examination of the blood showed that he was infected with the aestivo-autumnal type of parasite. He was given quinine treatment and discharged as cured, but returned several days later with another attack. The other members of the household, consisting of two sisters and a brother, were then examined and found to be infected with the aestivo-autumnal type, though with the exception of an enlarged spleen they showed no evidence of the disease. They were all treated with quinine till their blood was sterile, and no further attacks took place.

Cases of transmission of malaria as the result of transfusion of blood have recently been reported by Oehlecker, of Hamburg, and Van Dijk, of Rotterdam, respectively. Oehlecker's patient was a woman, aged 55, who was transfused for severe anaemia secondary to an operation for nasal polypi, the donor being her son, a vigorous man of 29, who had formerly been in the tropics (West Africa), but had never had an attack of fever. Fourteen days after the transfusion the woman developed an attack of double tertian, ring forms being found in her blood. In the case of the donor a violent shivering attack developed 36 hours after the transfusion, so that the removal of a large quantity of blood (1 litre) had a provocative effect. No parasites were found in his blood, but the examination was not made until three weeks after his attack. Van Dijk's patient was a nursing sister in a Rotterdam hospital, suffering from a severe attack of influenza, whom he transfused with the blood of another sister convalescent from the disease. Three weeks later the patient developed a typical attack of tertian malaria, although she had never had a previous attack and there was no other case of malaria in Rotterdam. It was then found that the donor had had an attack of malaria seven months previously and malarial parasites were found in her blood.

Symptomatology. From a study of the **time incidence** of a thousand simple tertian malaria paroxysms, Stephens, Yorke, Blacklock, and Macfie concluded that 90 per cent. of the paroxysms in simple tertian malaria occur during the hours of activity, i. e. 7 a.m.–6.59 p.m. The maximum number of paroxysms occurred at 2 p.m. Alteration of the period of activity by one hour, the result of the adoption of summer time, produced a corresponding alteration in the time of incidence of the paroxysms.

Hajra records five cases of a **haemorrhagic type of malaria** characterized by the following symptoms: frequent liquid haemorrhagic stools in large quantities, containing shreds of mucous membrane but no faecal matter, bilious vomiting, sometimes associated with haematemesis and haematuria, clammy extremities, and an almost imperceptible pulse. In three cases examination of the blood showed the malignant tertian parasite and in one a mixed infection; the other two cases were clinical malaria with an enlarged spleen. All the cases recovered under treatment by intramuscular injections of quinine, subcutaneous injections of pituitrin, and calcium chloride internally.

Fróes, of the Bahia Faculty of Medicine, reports a case of simple **quartan malaria** in a negress, aged 20, which appeared in the form of urticaria of two days' duration followed by an interval of two days in which she was free from the eruption. Examination of the patient showed tenderness of the liver, slight enlargement of the spleen on percussion, and the presence of *Plasmodium malariae* in the blood. The condition was cured by quinine.

Simons, of Dusseldorf, records a case of quartan fever remarkable for the fact that the small number of parasites was in striking disproportion to the severity of the symptoms. The cold stage, which generally lasts half an hour to two hours, was limited to a few minutes. The hot stage, which on the average lasts from four to eight hours, lasted only one or two hours, and was accompanied by an extraordinarily severe attack of sweating. While the duration of the whole attack in mild cases is normally from six to twelve hours, in this case very severe attacks in which the temperature rose on four occasions to 107·6 and once to 110·2 lasted from a quarter to half an hour. Quartan fever being usually a mild disorder, Simons considers that the course of the disease, the severity of the attacks, and the powerlessness of treatment render the case unique in the literature of malaria.

According to Massari, who records a case in a man aged 23, most of the reported cases of **rupture of the spleen** in malaria have been discovered only at the autopsy. In some districts of India malarial rupture of the spleen is so frequent that Crawford found 477 examples among 3,884 autopsies or 4·45 per cent. On the other hand, reports of cases in which an operation has been performed are extremely rare, this being due to the circumstances of life in the tropics and the superstition and indolence of the natives. Noland and Watson (1913), who, during the construction of the Panama Canal, operated on three cases of rupture of the spleen among 23,000 malarial patients, state that the patients were able to continue their work for a certain time after the rupture had taken place. In addition to his own case, in which operation was successful, Massari has collected 20 other cases of operation for rupture of the malarial spleen, 14 of which recovered and 6 died. The prognosis depends on the rapidity with which the operation is performed. Owing to the large number of cases of malaria resulting from the war the possibility of rupture of the spleen following a slight injury should always be borne in mind. Malarial patients and their friends should therefore be warned as to the vulnerability of the spleen, and instructions should be issued to first aid posts, police stations, &c., so that surgical assistance may be obtained without delay.

According to Hennessy, who has observed 17 cases of rupture of the spleen, in only two of which the organ was of normal size, the rest weighing from 10 to 37 oz., 151 cases of rupture of the spleen were officially recorded for the four Federated Malay States during the four years 1915–19, this high figure being indirectly due to malaria. The greater liability of the malarial spleen to rupture is shown by the fact that during the years 1900 to 1909 the number of cases of rupture of the spleen recorded for the State of Selangor was only six, whereas from 1909 to 1919, owing to a great influx of labour into the country and a great increase of malarial fever, a corresponding increase in the number of cases was recorded, viz., 53 cases.

Jebens remarks that in many cases of latent malaria changes take place in the **liver and pancreas** indicated by urobilinuria, enlargement of the liver, and glycosuria, which it is difficult to explain until the cause is revealed by provocative measures, such as the quartz lamp or adrenalin, when malarial parasites are found in the blood. As soon as the nature of the condition is recognized and quinine has been administered, the symptoms subside. But if for any reason the malaria is not cured, regressive changes may succeed the initial hyperaemia in the liver, and cirrhosis supervenes. In like manner glycosuria may be converted into diabetes mellitus when a condition of protracted and relapsing malaria persists, giving rise to gross organic changes possibly in the islands of Langerhans. Jebens alludes to a case reported by Jacobson in which fatal diabetic coma developed a week after the last attack of malaria. Burdel has also recorded cases in which after repeated relapses glycosuria became permanent and independent of the attacks of malaria.

Furno refers to the papers of Fraga (vide *Medical Supplement*, 1918, **1**, 446), Dudgeon and Clarke (*Medical Science*, 1919, **1**, 260–1), and others on involvement of the **suprarenals** in malaria, and records a case in a man, aged 42, who about six months after his first attack of malignant tertian developed all the signs of Addison's disease, such as adynamia, fall of blood-pressure, and pigmentation of the skin and mucous membranes. Suprarenal opotherapy was followed by considerable improvement, and the patient was able to resume his hard work as a porter. The patient was a vigorous man without any family or personal history of tuberculosis, and careful examination of the chest, including the use of X-rays, failed to reveal any signs of tuberculosis. Furno therefore concludes that the syndrome of Addison's disease in this case was due to malaria.

Parsons draws attention to the **peritoneal syndrome** in malaria which is characterized by general abdominal pain and tenderness, some distension, and muscular spasm. In some cases these signs are distinctly localized, the right side showing marked rigidity as compared with the left, or the upper right quadrant may be involved, simulating a gall-bladder infection. Parsons suggests that the symptoms are due to extension of the perisplenitis to the diaphragm. The claim that the symptoms are of an inflammatory nature is supported by the presence of leucocytosis.

In the course of two months Enright saw ten cases of malaria, chiefly of the subtertian variety, in which the onset was accompanied by **ascites**, oedema of the feet, puffiness of the face frequency of micturition, and vague discomfort over the lumbar regions. All responded readily to quinine. No specimen of urine contained casts, but there was invariably a very appreciable amount of albumin which quickly disappeared after quinine treatment.

Coullard-Descos suggests that the occurrence of **oedema** without albuminuria in the course of malaria is possibly due to changes in the thyroid gland like the oedema met with in cachexia strumipriva.

Coda, of the Turin University Medical Clinic, records two cases of malaria in men aged 42 and 56 respectively, presenting the blood-picture and all the other manifestations of **pernicious anaemia**, including achylia gastrica, in whom complete recovery took place under quinine treatment.

Fonzo reports two cases of **musculospiral paralysis** of malarial origin in children. In one case the paralysis developed during an attack of benign tertian, and in the other case about a month after an attack of malignant tertian. All other causes for the paralysis but malaria could be excluded in both cases.

Sabatucci records two cases in soldiers who, after contracting malaria in Albania, began to suffer from paraesthesia and weakness in the lower limbs. Intermittent claudication then developed, and finally complete **paraplegia**, bed-sores, and trophic ulcers. There was a loss of all modes of sensibility, which was most marked in the distal segments and less in the proximal ones. The paraplegia, which was at first flaccid, later became spastic and under vigorous quinine treatment gradually improved until only a slight paraparesis remained in one case, while in the other the symptoms were a little more pronounced. The condition is attributed by Sabatucci to spinal softening due to malarial arteritis in the lower part of the dorsal cord and some of the lumbar segments.

According to Porot, of Lyons, who refers to the recent work on **malarial meningitis** (vide *Medical Science*, 1919, **1**, 59–60), primary malaria may sometimes assume the form of acute meningitis with continued fever in children or young subjects, but a meningeal reaction is common during a relapse. The symptoms may be intermittent like the fever, attacks of nuchal rigidity, vomiting, and dissociation of the pulse and temperature occurring every two days, but as a rule the meningitis is the result of several attacks of malaria. The patient is sunk in a meningeal coma which is curable or fatal according to the case and the rapidity with which treatment is applied. Lastly malarial meningitis, like all other forms of acute meningitis, may have sequelae such as pain of radicular distribution, muscular atrophy, and ankle clonus.

Marinesco records a fatal case of myoclonic **encephalomyelitis** in a woman, aged 26, in whom the clinical appearances and the slight degree of spinal lymphocytosis suggested the diagnosis of epidemic encephalitis. The malarial origin of the condition, however, was shown by examination of the blood and the characteristic changes in the central nervous system.

Conti reports the case of a female child, aged 1½ years, admitted to hospital with acute nephritis, who developed left **hemiplegia** the day before death. The autopsy showed a large haemorrhage in the right cerebral hemisphere and degeneration of the vessel walls on microscopical examination. The haemorrhage was attributed by Conti to a chronic nephritis of malarial origin.

Constantinesco, of Bucharest, records five cases in soldiers who presented a **cerebello-spastic syndrome** characterized by disturbance of equilibrium, asynergy, adiadokokinesis, nystagmus, dysarthria, exaggeration of the reflexes, and ankle clonus. The symptoms were undoubtedly due to malaria for the following reasons: (1) They appeared after definite attacks of malarial fever. (2) Examination of the blood always showed *Plasmodium praecox*. (3) Quinine caused the symptoms to disappear.

Congenital malaria. Cuadra, of Nicaragua, records the case of a woman aged 26, with a past history of malaria, who gave birth to a child on January 19. The labour was difficult and forceps were applied. On January 21 the mother had an attack of shivering with a temperature of 104° F. The child's temperature also rose to 104°, and examination of both the mother's and infant's blood showed the presence of *Plasmodium vivax*.

The mother was treated by injections of quinine and the infant was given 1 c.cm. of euquinine by mouth every hour. Both recovered. Rabinoff also reports a case of congenital malaria in an infant a few hours old whose mother had suffered from chronic malaria with occasional acute exacerbations. Examination of the infant's blood showed tertian parasites. Quinine in gr. i doses every two hours was ordered. There was only a slight rise of temperature on the third day, and no recurrence took place.

In a paper on **malaria in children** at Smyrna, Veras states that though malaria is very prevalent throughout Asia Minor the town of Smyrna was relatively immune before the war, only 3 per cent. of the children brought to his out-patient department from 1906–13 suffering from the disease, as compared with 11 per cent. from June to December 1920. The largest proportion of his cases occurred between the ages of one and two years. The form of malarial fever observed was the quotidian type, which is the most frequent at Smyrna. A characteristic tertian was met with in only eight out of 88 cases seen between January and December 1920. Veras never encountered the quartan type. Concetti's dictum that malaria in children has a greater tendency to chronicity than in the adult is confirmed by Veras, 66 of whose cases belonged to the chronic form. The liability of malaria to affect the nervous system in children was exemplified by the frequency of convulsions as an initial symptom and by the tendency of the disease to simulate meningitis. Gastro-intestinal disturbances were a frequent complication in young children, as in the cases observed by Rabinoff.

According to Rabinoff, who records her experiences of malaria among children in Palestine during 1918, the outstanding features of the disease in children are as follows: The chill is less frequently an initial symptom. On the other hand, there is a greater tendency to convulsions and other nervous symptoms, such as restlessness, twitchings, fretfulness, or drowsiness. In children under two years gastro-intestinal symptoms are very frequent. The interval between the attacks is usually marked by a striking return to a normal appearance. Lastly, there is a much greater tendency to irregularities of temperature than in adults.

James states that among the civilians who contracted malaria in England between 1917 and 1919 no fewer than 75 per cent. were children. In the great majority the symptoms were quite typical, but more severe than in most of the indigenous cases in adults. In some cases an irregular temperature and absence of characteristic attacks of shivering and sweating caused delay in diagnosis, and in a few the symptoms were so mild that the illness was not observed by the parents, but was discovered during special inspection of school children. James is opposed to the view that children suffer less severely from malaria than adults, and points out that in highly endemic localities the malarious children who appear on superficial examination to be healthy are those who after much chronic ill-health have succeeded in surviving repeated attacks until a tolerance to the effects of parasitic invasion has been acquired. In places where children above the age of 10 show this tolerance the mortality among infants and children under five or six years of age is very high.

Malaria and amoebiasis. Job and Hirtzmann, after alluding to their previous papers on the frequent association of malaria and specific or non-specific intestinal disturbance (vide *Medical Science*, 1919, **1**, 263), attribute this association to at least three factors, viz. (1) the special susceptibility of the intestine in hot countries; (2) the frequent involvement of the intestine in malaria; (3) the predisposition which the malarial parasite and the dysentery bacillus create for one another. The amoeba of dysentery and the malarial parasite also tend to combine their pathogenic effects. Malarial symptoms, however, do not usually occur simultaneously with those of amoebic dysentery, but malarial paroxysms appear as a rule during the decline of an attack of amoebic dysentery. The writers come to the following conclusions: (1) In a malarial country the association of amoebic dysentery and malaria is frequent. (2) It is most important not to overlook this combination. Although treatment by quinine and emetine will completely cure a certain number of cases, it is not infallible, and, in spite of energetic measures, intestinal or hepatic amoebiasis complicated by malaria is inevitably fatal in some cases.

Malaria and syphilis. Noel records a case of reactivation of syphilis by an attack of pernicious malaria and manifested by periostitis localized in the callus of an old fracture of the tibia.

Diagnosis. Quarelli of Turin, records the results of his observations on about 600 cases in which he had employed provocative injections. The drugs used were adrenalin 1 in 1000 solution, strychnine 3–5 mgm., 8–12 drops of 1 per cent. alcoholic solution of nitroglycerine in 2–3 c.cm. of distilled water intramuscularly, emetine hydrochloride intravenously or intramuscularly in 12 cgm. doses and arsenobenzol 0·8–0·10 gm. intravenously. Antityphoid or antiparatyphoid vaccine subcutaneously, intravenous injection of 10 c.cm. of horse serum, and intramuscular injection of 10 c.cm. of cow's milk were also used. The most efficacious drugs for producing an attack were nitroglycerine, with which positive results were obtained in 72–4 per cent., emetine hydrochloride, and strychnine, with each of which attacks were produced in 59 per cent., and adrenalin, which was successful in 49 per cent.

Haider used benzol as a provocative agent for latent malaria as recommended by Henszelmann (vide *Medical Science*, 1919, **1**, 264), but with entirely negative results, although he employed as large doses as 12·0 gm. per diem. In no case was the administration of the drug followed by a characteristic rise of temperature or a typical malarial attack with appearance of plasmodia in the blood.

Marx, who devotes his Paris thesis to a consideration of the Wassermann reaction in malaria, states that 29 writers have published a more or less detailed account of the results of the reaction in 1156 cases of malaria. Excluding two cases in which malaria was associated with undoubted syphilis, the number of positive cases was 322 or 28 per cent. Out of 611 cases in which the reaction was tested during an acute attack, positive results were obtained in 274 or in 45 per cent. A positive Wassermann reaction does not appear to have been found in chronic malaria. The reaction remains positive for from about a month to six weeks after the acute attack. It is less frequently positive in malignant forms than in others. Occasionally it becomes negative as soon as the parasites disappear from the blood. As quinine appears to have a very definite influence in transforming a positive into a negative reaction, Marx recommends that in districts where malaria is particularly prevalent a positive Wassermann reaction in malarial subjects should not be regarded as evidence of syphilis until after a quinine treatment of about six weeks (vide also *Medical Science*, 1919, **1**, 61–2).

Treatment. Johnson and Gilchrist made a statistical investigation of 18,731 cases of malaria returned from the German East African campaign and admitted to military hospitals in South Africa. The earlier records of this series frequently showed a dosage of quinine of 5 or 10 gr. daily, which was commonly associated with repeated relapses and progressive anaemia. In November 1917 definite instructions for the routine treatment of malaria were issued, all ordinary cases, irrespective of type, being ordered 10 gr. of quinine in solution three times daily for three weeks, followed by the same dose twice daily for one month and then 10 gr. daily for two months. The increase in the number of days in which quinine was administered was associated with a reduction in the number of days in hospital. It was found that mixed infections of benign tertian and malignant subtertian were more resistant to treatment than either benign tertian or malignant tertian, and that benign tertian was as resistant or even more resistant than malignant tertian when the question of parasitological or clinical relapse was taken into consideration.

Macfie treated 62 native schoolboys, aged from 5 to 18 years, at Accra in the Gold Coast, West Africa, by oral administration of quinine sulphate gr. x. daily for two consecutive days only. All the boys appeared to be healthy and were found to be infected with malignant tertian malaria only on blood examination. This dose of quinine was sufficient in every case to cause disappearance of the parasites from the cutaneous blood in one or two days. After this treatment parasites reappeared in the blood in the majority of cases. The percentage of parasitic relapses was highest in the age-group comprising boys from 12 to 14 years. Only one of the 62 boys was definitely known to have had a febrile relapse. Though possibly some of the youngest boys may have had malarial attacks which were not reported, the regularity of attendance at school of the majority of the boys showed that the amount of illness accompanying the large number of parasitic relapses was very small. The number of relapses both parasitic and febrile was less numerous than in the case of the young native children or the adult Europeans, but more numerous than in the adult natives, probably owing to a development of tolerance in the latter.

According to Johnson, Gilchrist, and Hay-Michel, neosalvarsan, salvarsan, neokharsivan, kharsivan, and galyl may be safely given intravenously in all forms of malaria if proper doses and precautions are observed. These preparations exert a marked parasiticidal action on the benign tertian parasite, but have no definite parasiticidal action on any stage of the malignant subtertian parasite. Generally speaking, the tonic effects of these preparations is well marked in all cases of malaria. Anorexia, lassitude, and debility soon disappear, and splenic enlargement subsides with great rapidity. These preparations are of value in addition to quinine treatment in chronic resistant infections and malarial cachexia. Three or four injections at weekly intervals are recommended.

Brau and Marque, who record three illustrative cases, have found that while quinine, even in intravenous injections, has little effect against the resistant forms of *Plasmodium falciparum*, intravenous injections of novarsenobenzol appear to be specially indicated in cases of malignant tertian in which crescents predominate, the action of the drug being to arrest the febrile attacks and cause the disappearance of the crescents. Commenting on Brau and Marque's paper, Abrami and Senevet maintain that, though the various substitutes for salvarsan are in many cases good adjuvants of quinine in the treatment of malignant tertian, they cannot replace it. Moreover, it is indispensable, in studying the therapeutical action of a drug, to take into account the spontaneous course of the disease, especially in the cases of malaria in which the relapses occur at very infrequent intervals.

According to Salotti, who has treated 23 cases, neosalvarsan is a specific in the treatment of malaria which is refractory to quinine. In the first place it causes a rapid regeneration of the blood by its stimulating effect on the haematopoietic organs. Secondly, in acute pernicious malaria it is an excellent adjuvant to quinine, because it strengthens the patient's resistance. Thirdly, it enables quinine treatment to be suspended when this is of little benefit or produces symptoms of intolerance.

D'Esterre records 20 cases of recurrent malaria, 12 of which were benign and 8 malignant tertian, successfully treated by a course of four intramuscular injections of novarsenobenzol (neokharsivan) without any further recurrences being reported. The first two injections consisted of 0·3 gm. in 5 c.cm. 0·5 per cent. sterile saline, and the last two injections of 0·4 gm. in 7 c.cm. 0·5 per cent. sterile saline. The injections were given at intervals of a week.

A combination of intramuscular injections of quinine with subcutaneous injections of 5–15 c.cm. of inactivated serum from carefully selected malaria convalescents is highly recommended by Seyfarth, who states that since he has employed this treatment he has had no fatal cases with the exception of two patients moribund on admission to hospital.

Sarailhé used the 'sérum hémopoiétique' of Carnot in malarial anaemias with good results. The serum was obtained in the following way: Rabbits of average weight of just over 3 kgm. were carefully tested for parasites, &c. They were then bled to the extent of 60 c.cm. and this was repeated five days later. The serum obtained from the second bleeding by centrifuging was put in the ice-chest and used the following morning, not more than eighteen hours later. It was given intravenously in every case. The complete course comprises from three to six injections, the dose rising from 25 to 40 c.cm. Fifty-three patients were treated, and none had a red cell count so high as three million. It was not uncommon for the injections to determine an attack of malaria with parasites in the blood some six or seven hours later.

Sarailhé claims that the good results are especially seen in the ensuing increase in the number of red cells, in weight, and in ability to sleep well, insomnia having been a troublesome feature in his cases. These results were quickly obtained and after only few injections, e. g. one a day for four successive days. It is also evident that the patients experienced much of the sudden increase of liveliness often seen after transfusions of blood. But the treatment is not curative of malaria and quinine therapy must be continued.

In four cases the treatment gave good results, but a rise in the number of red cells was no sooner obtained than it was destroyed by a malarial paroxysm. Certain cases of malaria were kept under observation as controls. Some of these showed quick rises in the number of red cells on quinine medication, but, by comparison with those who had serum treatment, were unable to maintain the increase in face of fresh malarial relapses. The serum cases, on the other hand, were found to maintain the position gained up to three months afterwards, this being the longest interval at which war conditions allowed the following of a patient.

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RELAPSING FEVER

Aetiology. According to Willcox, the danger of infection by the breath, excreta, blood, &c., from a patient suffering from acute symptoms and who has been effectively deloused, is greater in the case of relapsing fever than in typhus. He has seen several cases in which those nursing relapsing fever patients have contracted the disease in spite of every precaution taken as regards lice, and he has met with two cases in which bacteriologists developed the disease after taking blood-films from relapsing fever cases, the usual incubation period intervening. A medical officer who accidentally got some blood on his hands, on which there were some abrasions, had an incubation period of five days. The spirochaete of relapsing fever may possibly gain entrance through the unbroken skin, like the spirochaete of haemorrhagic jaundice.

Cragg, of the Central Research Institute, Kasauli, states that relapsing fever occurs over the greater part of India with the exception of Assam, Bengal, and Madras. Isolated cases and small outbreaks are frequently reported among troops and followers, and in jails in Northern and Central India and in the Deccan. Its occurrence is not determined by climatic conditions, for it is not an uncommon disease in states so dissimilar as Bombay and Quetta. The disease appears to be more serious in the United Provinces than elsewhere. Unlike the relapsing fever of Europe, North Africa, and America, where it is more prevalent in winter, the epidemics in the United Provinces occur mainly in the hottest part of the year, in the months of March, April, and May. Although the rôle of the louse has been fully established in the winter epidemics of relapsing fever in Europe, North Africa, and America, Cragg maintains that it is very unlikely that this parasite is the transmitting agent in the hot weather epidemics, when lice are comparatively scanty in number. He considers that their scarcity accounts for the failure of the disease to take hold in the Ahmednagar camps, where most of the cases occurred singly or in small groups, in marked contrast with the outbreaks in the Bijapur Jail in 1901 with 323 cases, and in the 'Deccan Gang' in 1902 with 210 cases, which were probably examples of classical relapsing fever transmitted by the louse. It is probable that the relative immunity of the troops from relapsing fever is due to the greater cleanliness of their habits as compared with those of the rural community from which they came.

According to Manson and Thornton, in their study of East African relapsing fever, the tick *Ornithodorus moubata* was the only carrier of infection in the Dar-es-Salaam area whereby the disease was spread. Other possible carriers, such as lice, bed-bugs, fleas, and chiggers, were investigated, but showed no evidence of any relation to the disease. The number of these insects did not bear any relation to the incidence of relapsing fever, nor was the *Spirillum duttoni* found in any of them.

Symptomatology. During 1917 and 1918 Caldwell had the opportunity of studying 125 cases of relapsing fever among British and New Zealand troops at the 27th General Hospital at Cairo. 69 cases were of the Egyptian or North African type and 56 of the Palestine type. In the Palestine type, which has not hitherto been described, the initial symptoms resemble those of the North African relapsing fever. Pain over the liver is more frequent, and the organ is more often enlarged, while enlargement of the spleen is the exception. The initial fever is considerably shorter than in the North African type, lasting two to four days and ending by crisis. Slight jaundice, often merely conjunctival, occurred in 25 per cent. of the cases. The average number of relapses in Caldwell's cases was 4·5 as compared with 1·35 in the North African type of the previous year, and treatment by kharsivan undoubtedly cut short the number in several cases. The apyrexial intervals were very irregular, and, unlike the North African type, there was little tendency to a regular periodicity, the intervals tending to become longer in the latter relapses, but not invariably so. Afebrile periods lasted from two to 27 days, but a relapse rarely occurred after 14 days and still more seldom after 21 days.

Newcomb describes an outbreak of 66 cases which occurred in the northern part of Mesopotamia in April–June 1918 with only one death; 65 of the cases were in men and 1 in a woman. In the duration of the attacks and intervals, as in the symptoms, the cases corresponded to the classical description given by Vandyke Carter in 1882, and those of most subsequent observers. In the cases which relapsed after a dose of neosalvarsan the relapse was delayed from 14 to 30 days (average 19 days) as compared with an interval of 5 to 12 days (average 6·8 days) in cases not treated with neosalvarsan. In view of the long interval Newcomb suggests that the 'relapses' were really reinfections, especially as little or no immunity is conferred by an attack.

In an article on the occurrence of relapsing fever in home hospitals, Hesse records four cases of soldiers repatriated from the Ukraine, and admitted to a hospital in Germany as convalescents from typhus, who subsequently developed peculiar rises of temperature. Examination of the blood in each case showed the presence of the spirillum of relapsing fever. In three cases the original disease was undoubtedly typhus, and the Weil-Felix reaction was still positive. In the fourth case the rise of temperature in the home hospital was a second attack of relapsing fever. Such cases indicate the necessity of thoroughly delousing patients on admission to home hospitals as well as of revising the diagnosis by bacteriological examination.

Gerstl, of the German Children's Clinic at the Prague Foundling Hospital, records a case of relapsing fever in an infant aged 8 days, in whom the disease ran a fairly typical course and was apparently cured by an intragluteal injection of 0·02 gm. neosalvarsan. The mother, who had an attack of relapsing fever at the time of her confinement, had recently come from Roumania, where her mother and grandmother were similarly affected, so that four generations were simultaneously suffering from the disease. As the child was separated from its mother immediately after birth, infection must either have taken place *intra partum* or have been transmitted by lice, but the former hypothesis is the most probable. Gerstl has not been able to find another example on record of relapsing fever in the new-born.

Strominger, of Bucharest, whose observations on the *urinary complications* of typhus have recently been mentioned (vide *Medical Science*, 1921, **4**, 196) states that relapsing fever, like typhus, fairly frequently affects the kidney and more frequently the bladder, as he has seen about 30 cases of vesical disorder in patients dating from six weeks to two or three months after the fever.

Monziols and Collignon found that in the great majority of their cases of relapsing fever a syndrome of *acute suprarenal insufficiency* developed during the twelve hours following the injection of novarsenobenzol, characterized by nausea and vomiting, profound asthenia, fall of blood-pressure, with discoloration of the skin and mucous membranes and the appearance of Sergent's white line. They attribute the condition to the sudden destruction of the spirilla by the arsenical treatment, whereby a large quantity of toxin is set free and renders the antitoxic function of the suprarenals insufficient. Since they have systematically injected 1 mgm. of adrenalin into every patient who has been given '914', they had never met with the syndrome. One patient who was not treated with adrenalin developed left hemiparesis and violent delirium at the same time as the suprarenal syndrome. The cerebrospinal fluid was normal, and there was no history of syphilis. Three injections of 1 mgm. of adrenalin were followed by considerable improvement the same evening, and the next day the paresis disappeared.

According to Löwy, who records a relatively mild epidemic of 119 cases in Belgrade in 1918, two of which developed paralysis of the circumflex nerve, *nervous complications* in relapsing fever are rare, transient facial palsy, haemorrhagic pachymeningitis, and apoplexy being the only ones given in the text-books. Koch and Lippmann have recently reported a case in which loss of consciousness was accompanied by abducens and facial paralysis, flaccid paralysis of the right arm, and bilateral Babinski's sign. The palsies all disappeared in a few days, being probably due to vascular obstruction caused by the spirilla or to inflammatory changes in the brain substance. Walko has recorded five cases with meningeal symptoms which ran a similar course. In one of Löwy's cases the increased reflexes and ankle clonus pointed to spinal involvement, while in the other the absence of knee-jerks indicated a peripheral process.

It may be noted that one of Newcomb's 66 cases developed facial paralysis, but he was unable to determine whether this was a mere coincidence or not.

Manson and Thornton also found that nervous lesions were extremely uncommon, as in a series of about 1,500 cases of East African relapsing fever observed in 1917 and 1918 not more than $\frac{1}{3}$ per cent. showed any sign of nerve involvement. Nervous complications in their experience always occurred late in the disease, seldom earlier than the sixth week after the disease had been diagnosed as relapsing fever. The lesions were of a transient nature clearing up in a time proportionate to the severity of the case and the nature and extent of the nervous tissue involved. The cases were classified into (1) those showing gross central nervous lesions, such as aphasia, complete facial paralysis, and hemiplegia, and (2) cases showing involvement of one or more cranial or spinal nerves.

Trantas records his observations on the *ocular complications* of relapsing fever in the military hospitals of Athens. (1) Conjunctival lesions. During the fever there was frequently congestion of the palpebral and bulbar conjunction. In four out of fifty cases the conjunctiva was markedly icteric during the fever and for some days later. (2) Corneal lesions. 23 out of 50 cases, or 46 per cent., showed superficial transient lesions almost always situated in the upper half of the cornea on one or both sides analogous to the renal lesions, as shown by albuminuria and the presence of granular casts which are so frequent and transient in relapsing fever. (3) Iridocyclitis with or without ophthalmoscopic lesions. (4) Ophthalmoscopic lesions such as retinal haemorrhage, chorioretinitis, and opacity of the vitreous apart from iridocyclitis.

Manson and Thornton found that iritis and iridocyclitis were very frequent in East African relapsing fever, both among Europeans and natives. The complication might occur at any period of the disease, but was unusual in the latter stages when the relapses had come to an end. Though the condition was usually bilateral, one eye as a rule was affected much more seriously than the other.

According to Costiniu, of Bucharest, the *aural complications* of relapsing fever assume almost the same form as in typhus (vide *Medical Science*, 1921, **4**, 196), but are less frequent, and recovery after operation is more rapid. The *laryngeal complications* of relapsing fever are much rarer than in typhus. In one patient who had relapsing fever and then typhus a polypoid growth on the vocal cord was found and successfully removed. Histological examination proved that it was of inflammatory nature. In another case an endolaryngeal phlegmon was opened and cured. Costiniu also saw two cases complicated by quinsy, in the pus from which Obermeyer's spirillum was found.

During a severe epidemic of relapsing fever in the winter of 1918–19 in Teheran, Post saw at least half a dozen cases of *costal caries* and heard of many more. The history given was of pain and swelling over the front of the chest during the illness, not subsiding during convalescence, with abscess formation a few weeks later. The upper and middle cartilages were attacked from the third to the eighth. The course of the infection was afebrile and marked by great indolence, resembling similar infection following typhoid. Post himself developed an abscess over the fifth right costosternal articulation, for which several operations were required, parts of the fifth, sixth, and seventh cartilages and ribs being removed. The site of infection, viz. the posterior aspect of the costal cartilages, and the low resistance of the cartilages themselves, are regarded by Post as accounting for the extensive burrowing which demands radical resection of the overlying tissues.

Treatment. From observations in the outbreak in Mesopotamia, Newcomb concluded that 0·45 gm. was the best dose of neosalvarsan for the treatment of relapsing fever. In 30 cases 0·3 gm. was given, and in eight of these subsequent relapses necessitated a further dose of 0·3 gm., and in one case two further doses, whereas in 20 cases which had 0·45 gm. in the first place no relapse occurred.

Del Prado confirms the remarkable efficiency of neosalvarsan in the treatment of relapsing fever, only two of the 362 cases under his care failing to show a complete cure under it, and these two cases left the hospital too early. He never had occasion to repeat the injection of 35 or 45 cgm. of neosalvarsan in 10 c.cm. of distilled water.

Manson and Thornton found that novarsenobillon 0·9 gm. gave the most satisfactory results in the treatment of East African relapsing fever. They recommend that it should be given on the first attack of the fever, or, failing that, on the first relapse. It should always be administered on the rise of temperature and never in the apyrexial period. If a further relapse should occur the dose should be repeated as before on the rise of temperature. The writers state that the native stands the administration of salvarsan or its substitutes well, and is not subject to the serious symptoms following its administration which are often observed in Europeans.

Peyre states that during the epidemic of relapsing fever in Roumania in the winter of 1916–17, when the supply of neosalvarsan ran out, intravenous injections of a solution of cacodylate of soda generally stopped any further attacks, though not so rapidly as neosalvarsan.

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J. D. R.

CONGENITAL DILATATION WITH HYPERTROPHY OF THE COLON

This was the title used by Hirschsprung, of Copenhagen, when describing in 1886 two cases in infants, and is that adopted in the 'Nomenclature of Diseases' by the College of Physicians. Many of the cases since published have been similar in type, the abnormality shows itself soon after birth and leads to an early death. In less extreme cases children survive in spite of obstinate bouts of constipation, alternating with several exhausting fluid motions. Such older children may be able to sustain the wide excision of the affected gut. More recently attention has been specially directed on the Continent, both in France and Germany, to adults, who beforehand had not been troubled importantly, although subjects of limited dilatation with hypertrophy of the colon. But under alterations in their diet, consequent on the war, or incidental to military service, obstinate constipation has set in, terminating in an attack of intestinal obstruction. Excision of all the affected bowel has proved the only method by which permanent relief can be given; whether excision is practicable in any particular patient depends upon the stage to which intestinal obstruction has advanced. The two patients first noted by Hirschsprung died at 11 months and 7 months respectively owing to the dilatation with hypertrophy of the colon, without any obstruction, the bowel being chiefly distended by gas.

Dalle Valle has published the account of a specimen placed in the Pathological Museum at Parma by Inzani, which demonstrates, besides the dilatation and thickening of the wall, the great increase in length of the colon in marked cases. A boy aged 5 had obstinate constipation from birth, defaecation occurred at intervals of 15–20 days, the abdomen became distended to a circumference of 82 cm. at the umbilicus. Death occurred from toxaemia. The length of the colon in the dry state was 182 cm., from the caecum to the hepatic flexure 37 cm., from the hepatic to the splenic flexure 33 cm., the sigmoid flexure was 83 cm. long. The ascending and transverse colon had a circumference of 37 cm., the upper part of the sigmoid 35 cm. The wall of the colon was of normal thickness except the sigmoid, which was enormously thickened; there were no naked-eye changes in the mucous membrane.

Now the average length of the large intestine in the infant is 43 cm., in an adult 120 cm.; the circumference of the colon in the adult varies from 20 cm. in the ascending colon to 14 cm. at the sigmoid flexure. There is little difference in the thickness of the wall, in a young child 1·2 mm., in an adult 1·5 mm. It is especially important to note from the point of view of surgical treatment that when the condition is well marked in young children death is occasioned by the exhaustion resulting from toxaemia, the gut being continually distended by foul gas. In adults the increased length occasions kinks and volvulus which induce intestinal obstruction.

In 1914 Barrington-Ward, in the course of a valuable account of observations at the Hospital for Sick Children, Great Ormond Street, directed attention to the necessity of distinguishing typical cases in young children from cases of faecal impaction consequent on spasm of the sphincters set up by anal fissure. Also impaction of faeces may occur above a valve in the rectum, as noted by Delbet. In the one case the impaction is relieved by dilatation of the anus, in the other by removing the valve from within the rectum. At the Hospital for Sick Children, between 1868 and 1912, there were 19 post-mortem examinations on typical cases; 16 were males, 3 females; 10 were under one year at death; 6 between 2 and 3 years; 13 deaths occurred under medical treatment; 6 after surgical operations. In all the sigmoid flexure was noted to be hypertrophied; in 2 the rectum was reported to be normal; in 5 the rectum was not mentioned, it may not have been examined. In none was there obstruction.

There has been no advance on the question of the pathology of the condition. An undue dilatation and thickening of the wall of the sigmoid flexure and upper part of the rectum exists at birth, together with an abnormal length of the sigmoid flexure. What is acquired after birth is an increase of the congenital deformity consequent especially upon the abnormal portions of the gut being continually distended by faecal gas. The co-existence of other congenital deformities in the infants have been noted, but there is no account of such complications in the cases submitted to surgical treatment.

Soon after birth there arises constipation with irregular distension of the abdomen; in cases dying soon after birth the meconium has not passed. Peristalsis becomes visible with loud gurgling. There is no motion until after repeated enemata. At 2 or 3 days' interval, or longer, crumbling dark scybala are passed, followed by several fluid motions, which exhaust the child, along with much foul flatus. Pain and vomiting are remarkable by their absence; the child takes food, although the appetite becomes more and more variable. Vomiting, when it occurs, is probably occasioned by the distension of the sigmoid flexure pressing up upon the duodenum.

The child presents a greatly distended abdomen, through the thin wall peristalsis is evident, and undue thickness of the colon may be recognized through the abdominal wall by pinching up the gut between the thumb and finger. Great dilatation of the sigmoid may be noted by the X-rays. Examination of the rectum with the finger shows that it is ballooned, without impaction of faeces.

The child gradually lapses into a hopeless state, the lower margins of the ribs tend to become everted, the persisting toxaemia causes wasting, exhaustion, and death. Before death the abdominal distension may cause oedema of the lower extremities and genitals; the ureters may be compressed and hydronephrosis follow; by pressure upwards through the diaphragm, the heart and lungs are impaired, and pneumonia may be the terminal complication. The mucous membrane of the dilated and hypertrophied bowel undergoes very little change until near the end, when, as in Hirschsprung's original cases, there may be found, as the result of colitis, erosions and submucous abscesses forming ulcers the size of pins' heads. If acute intestinal obstruction supervenes in a child, this proves to be due, in particular, to the increased length of the bowel rather than to the dilatation and hypertrophy of the wall; a kink or volvulus suddenly forms.

The only treatment which the pathology and clinical course of the affection in the child shows to be applicable is that of excision of the abnormality with the union of unaffected gut above to the upper end of the rectum below. But excision has not yet been shown to be practicable in a young child, not only because the child cannot sustain the operation, but because of the thinness and friability of the intestinal wall, so that suturing cannot be done effectively. There is one possibility of giving relief in a young child, if the diagnosis is made early, before there is marked distension and toxaemia, viz. to diminish the length and reduce the lumen of the bowel by longitudinal plication.

It is hopeless to wait until there is great distension or signs of intestinal obstruction, and then to make a faecal fistula. A faecal fistula does not relieve the accumulation of foul gas.

The experience of the reviewer has unfortunately been mostly concerned with such children, already suffering from acute obstruction. The following case, however, happened whilst this article was being written.

A boy, aged 5½, with a characteristic history and signs, had been under medical treatment in the hospital, during which his condition remained stationary but without increase of weight. Soon after discharge he was readmitted with threatened signs of intestinal obstruction. He was pale and thin with an abdominal girth at the umbilicus of 54 cm., the anus patulous, the rectum ballooned. Upon making a median hypogastric incision normal but dilated coils of small intestines were all that could be seen until the incision was extended above the umbilicus, when a dilated and thick-walled sigmoid flexure was found bulging into the epigastrium. It became necessary to let out all the small intestines, to gather them up and swing the mass round from the left over to the right side. Then the sigmoid flexure, which had undergone about half a turn in the direction of a volvulus, could be untwisted and spread out over the pubes. By the time that the small intestines had been replaced the boy had become very pale, with dilated pupils. The sigmoid flexure was at least double the normal length and its wall double the normal thickness. It was somewhat inflamed and friable in consistency. The gut was plicated by two longitudinal continuous sutures. Each stitch diminished the lumen transversely by about 1 cm., and, the distance between adjacent punctures with the needle being about the same, each stitch shortened the length by 1 cm. At the end the sigmoid flexure appeared reduced to about the normal, whilst the general condition of the patient had become somewhat better, assisted by continuous subcutaneous infusion of salt solution. Apparently the descending colon was dilated but not elongated, the transverse colon dilated but not thicker than normal or longer than usual.

The boy recovered from the operation and the bowels moved well on the second day.

In the case of older children Barrington-Ward reported that Arbuthnot Lane had succeeded in excising the whole colon.

Case I. A boy, aged 12, had the ileum divided and implanted into the commencement of the rectum. The whole of the intervening bowel was then cut out. Unfortunately the ligature applied to the left colic artery slipped off and so much blood was thus lost that in spite of intravenous infusion death occurred on the third day. There was no peritonitis; the rectum was hypertrophied even more than the pelvic colon.

Case II. A boy of 6 had the ileum implanted into the commencement of the rectum; there was much improvement for some time; the constipation recurred. Four months after the anastomosis the intervening gut was excised, after which the bowels were normally opened.

Case III, a boy of 10½, and *Case IV*, a boy of 3, had the ileum implanted into the rectum, and the bowel excised, all at one operation. Both recovered.

Case V. A boy aged 9 had the transverse colon implanted into the rectum, then the descending and pelvic colon excised. Improvement followed, the bowels moving daily by the aid of paraffin.

Tewfik reported the case of a boy aged 10 in whom complete obstruction had supervened upon obstinate constipation, due to an enormously dilated sigmoid flexure and rectum. An artificial anus was made in the left inguinal region and the bowel below washed out. Six weeks later the descending colon was united to the rectum and the sigmoid flexure excised. The general condition was much improved but there was an intermittent faecal fistula.

Hoffmann reported two cases of children operated upon by Payr in Leipsig.

Case I. A girl aged 5¼ was noted soon after birth to have a distended abdomen. During the first year there was constipation up to two days relieved by soap suppositories, &c., much foul flatus escaping. The appetite was variable, with a tendency to pica. For the next three years, about every three days, there occurred several foul loose motions. Gradually the abdomen became so distended as to overhang the pubes. The girth at the umbilicus was 56 cm. the height of the child being 89 cm. and the weight 11·7 kilos. At the operation the sigmoid loop was found to be 60 cm. in length and thickened to the size of a woman's wrist. A constriction was divided and some adhesions separated at the junction of the sigmoid and rectum, after which a tube was passed up from the anus, when mainly gas was evacuated. After this the patient became worse, with vomiting and a failing pulse, so the sigmoid flexure was opened and some scybala removed, but the child died 7 days later.

Case II. A boy of 7 had been distended from birth with obstinate constipation for days together, after which crumbling scybala and several liquid stools with foul gas were evacuated. Payr brought out the elongated and distended sigmoid loop and 8 days later cut the loop away. Forty-three days later an end-to-end union was made, but a faecal fistula recurred which necessitated a further resection. Nine months after the commencement of surgical treatment the boy had a normal motion once or twice a day.

In none of Payr's cases could excision be done offhand owing to the patient's general condition.

A number of cases have been published of late of adults suffering from complications supervening upon slighter degrees of congenital dilatation, hypertrophy, and elongation of the colon.

The long history of a case recorded by Makins shows that excision is indicated whenever practicable. A woman of 51 had had for a year increasing constipation, at intervals she had vomited; she had not been relieved by medical treatment: (1) In 1904 a dilated sigmoid was found and a lateral anastomosis was established at the base of the loop. (2) In 1905 a volvulus occurred, so the sigmoid loop was excised and an end-to-end union made; (3) In September 1906 a volvulus of the descending colon was untwisted and anchored. (4) In December 1906 the dilated descending colon was first punctured and then freed from its anchorage. (5) This gut becoming again distended, it was punctured and then plicated. (6) Attacks between July and November 1909 were relieved by medical treatment. (7) After death, in April 1910, the pelvic colon and upper part of the rectum below the anastomosis were found greatly dilated; the gut above was in good condition, there was no peritonitis or peritoneal adhesions. Throughout, the main feature had been accumulations of gas.

Lachmann's case, a man aged 26, had been troubled from childhood by obstinate constipation lasting 5–6 days and only relieved by repeated enemata. The sigmoid was found distended to the size of a bladderfull of lard, with a wall 3–4 mm. thick. A length of 35 cm. was excised and the colon in the region of the splenic flexure joined to the end of the sigmoid flexure. Recovery was delayed by a faecal fistula; after this had closed the bowels acted spontaneously.

Pauchet described the following cases:

Case I. A man aged 26 had had from infancy prolonged periods of constipation alternating with exhausting evacuations. On being called up for active service two attacks of intestinal obstruction supervened. At the first operation a volvulus of an elongated and dilated sigmoid flexure was reduced and plicated. At the second, the volvulus having recurred, the volvulus was untwisted and the loop sutured to the abdominal wall. The chronic condition persisted, the sigmoid became so dilated as to occupy most of the abdominal cavity; it was excised and the lower end of the descending colon united to the upper end of the rectum. The patient got up at the end of a fortnight.

Case II. A male aged 17, but having the appearance of a boy of 12, had had since infancy obstinate constipation, with threats of intestinal obstruction, but no previous operation. The sigmoid flexure was found to be 15–18 cm. in diameter and about 60 cm. in length; the descending colon was also dilated. The sigmoid flexure was alone excised; the dilated descending colon determined the formation of a faecal fistula above the level of union.

Case III. A woman of 35 had a volvulus of the large intestine for which a caecal anus was first made. Some weeks later the sigmoid flexure was excised, but a volvulus of the descending and transverse colon recurred. Thereupon the ileum was joined to the rectum and the colon removed. After temporary retention of gas in the small intestines the patient made a good recovery.

Guyot's case was also brought to a head on active service. The man, aged 28, was attacked by obstinate constipation, 15–20 days passing without a motion. Colic and distension by flatus kept him continually in hospital until he was discharged with the curious label 'bacillose péritoneale'. The abdominal distension caused wasting; eversion of the margins of the ribs and the obstinate constipation persisting after discharge prevented him from retaking up his post of ship's steward. In December 1918 the colon distended by gas occupied most of the abdomen from the diaphragm to the pelvis and a faecal fistula was established. This afforded little relief, and two months later the colon was found distended to the size of a man's thigh from the hepatic flexure down to be directly continuous with a dilated rectum. A caecal anus was made, the bowel down to the rectum excised, and the cut ends closed, the intention being to join the ileum to the rectum later on, if the patient recovered sufficiently.

Michon and Okinczyc operated on a woman aged 23, who from infancy had had obstinate constipation, generally lasting 5–6 days, but extending at times up to 12–17 days. One year before a caecal fistula had been made from which chiefly gas escaped. On exploration the dilatation was found to involve the descending colon and splenic flexure, so this was excised and the transverse colon joined to the rectum; at the same time the caecal fistula was closed. The result was good; the patient had two motions a day without laxatives.

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THE CEREBELLAR SYMPTOM-COMPLEX AND ITS SIGNIFICANCE

It is just upon a hundred years since Flourens published his classic researches upon the cerebellum, and in the century now elapsing a vast amount of experimental, clinical, and pathological work has been devoted to this subject; indeed, there is probably no part of the central nervous system which has been more extensively investigated than the cerebellum. Nevertheless, no generally accepted or completely satisfactory theory of its functions has yet been formulated, and the numerous writings on the subject show a degree of difference of opinion which indicates the extreme difficulty and complexity of the problem. The line of approach adopted by both experimental and clinical investigators of cerebellar functions has consisted in the study and analysis of the symptom-complex resulting from lesions of the cerebellum, either produced experimentally, or by disease or injury. When we review the experimental work we find that it does not differ very much in its methods or resources from clinical investigation, being confined to the simple observation of animals in whom lesions of the cerebellum and of its afferent and efferent paths have been produced. Indeed, in the intelligent co-operation of his patient, which the clinician often enjoys, he has had an important advantage over the experimental worker, who, on the other hand, could choose the site of his lesions and verify their extent subsequently in a manner impossible for the clinician. However, on the whole, both groups of investigators have employed similar methods, and even the most recent work on the subject is little more than a repetition of the pioneer researches of the last century.

It has been a principal object, then, with all workers in this field to study the symptom-complex of cerebellar lesions, and from its analysis to reach a satisfactory theory of cerebellar functions.

It is with some recent studies of this nature that we are concerned in this review.

Before we proceed to discuss the symptom-complex in detail, there are some general observations to be made. It has been finally established that cerebellar symptoms are purely motor and not based upon any form of sensory disturbance (Gordon Holmes). The problem of cerebellar function, therefore, involves the study of certain aspects of the co-ordination of movement. When the pioneer researches were carried out there was little exact knowledge of the factors underlying the motor co-ordination of the organism, and it is surprising that, with such vague and fragmentary information on these points as they possessed, the workers of the nineteenth century achieved such solid and valuable results. Within the past twenty-five years, however, an admirable series of refined and minute analyses of the modes of nervous activity has been carried out by Sherrington, Graham Brown, Magnus, and others. In this way a wealth of exact knowledge has been placed at our disposal in respect of the various factors underlying the co-ordination of movement. This being so, the vague conceptions and the loose terminology which were an inevitable handicap to past generations of workers in this field are no longer obstacles in our path. There are now scientific conceptions and an exact terminology into which we may translate the results of our clinical observations without fear of confusion or want of precision.

It is, therefore, the more astonishing that even the most recent clinical and experimental investigations have left these magnificent resources practically untouched. The results of this strike us at once when we come to study the literature on the cerebellar symptom-complex, for we find that underneath a very real measure of agreement as to the facts of observation there lies serious difference of opinion in the matter of nomenclature and interpretation. Authorities differ widely as to what are the fundamental defect symptoms in cerebellar lesions and as to the relationship of the various clinically observed disorders of movement to these essential defects, and to each other. Further, the terminology used is not uniform, nor does it embody clear conceptions. Take the case of atonia. For Luciani and Gordon Holmes this is an essential symptom, but for Babinski and André-Thomas it is neither essential nor of common occurrence. However, it is clear that the terms ‘tone’ and ‘atonia’ have such vague and diverse meanings to these writers that there can be no possible agreement between them as to the presence, characters, or significance of atonia. In the discussion of every aspect of cerebellar ataxy, the same confusion and lack of precision obtains.

So serious a criticism will probably not pass without challenge, but it does not lack abundant confirmation. Let us then review the symptomatology of cerebellar lesions as it has been described for us by such authorities as Luciani, Babinski, André-Thomas, and Gordon Holmes, to see what is definitely established, and to resolve, as far as is possible, the conflict of opinion which so obscures the value of their observations.

Luciani on cerebellar symptoms and functions. For Luciani the essential cerebellar defect symptoms are atonia, asthenia, and astasia. *Atonia* is seen as a diminished resistance of the limb muscles to passive flexion and as a tendency of the limb to give way under the subject, owing to sudden relaxations of the muscles. An additional result of this is seen in walking, where, during the flexion phase of the step, premature relaxation of the extensors causes the foot to be lifted over-high, and conversely, during the extension phase, premature flexor relaxation causes the foot to be planted on the ground with a stamp. This manifestation of atonia he calls *dysmetria*. *Asthenia* is seen as a tendency in cases of unilateral cerebellar lesion to fall to the affected side and as a disinclination to use the affected limbs. It depends upon a diminution of the active tension of the resting muscles, which normally ensures the proper force, form, and duration of a contraction. *Astasia* is the term used to describe the oscillations and jerkiness of movement seen in cerebellar cases. It is due to an absence of the normal fusion of the elementary motor impulses to the muscles, which should ensure a steady and continuous muscular contraction. Luciani adds that 'it is practically impossible to consider these three defects separately and apart. Astasia, in which the deficiency of static action is expressed, is usually held to be a natural effect of asthenia (*tremitus a debilitate*): asthenia, by which the loss of sthenic effect in the activity of the muscles is expressed, appears to be related to the atonia observed during their repose . . . it may be assumed that they are only three different extrinsic manifestions of a single process, though there may be no constant relation between their intensities'.

Cerebellar ataxy is a composite affair and results from these defects and from voluntary efforts to overcome them. It is not a true inco-ordination, since a dog deprived of its cerebellum and thrown into water can swim perfectly. For Luciani the cerebellum is simply a small independent co-adjutant reinforcing organ co-operating with the main cerebrospinal system in the motor taxis of the organism. It has no specific field of action of its own, and is not a co-ordinating or equilibrating organ. By its tonic, sthenic, and static action it ensures (*a*) the proper tension of the neuromuscular organs at rest; (*b*) the development of energy in them during action; and (*c*) acceleration of the rhythm of elementary motor impulses, thus ensuring a steady and continuous contraction of the muscles.

Babinski on the cerebellar symptom-complex. While Luciani's conclusions were based upon animal experiments, Babinski's descriptions are the result of clinical study. The apparent weakness or *asthenia* of cerebellar patients is not a true weakness, but simply the result of the violence of their disordered movements, which involve excessive expenditure of energy ('gaspillage d'énergie'). *Atonia* is an unimportant and occasional symptom, a simple matter of muscular softness and flaccidity to manipulation. The essential elements of the symptom-complex are dysmetria, asynergia, discontinuity of movement, and adiadokokinesis. *Dysmetria* consists in excessive and ill-proportioned movements. The patient commonly overshoots the mark (hypermetria). Babinski thinks that this fundamental cerebellar defect can best be explained by supposing that normally the cerebellum exerts a 'braking action' ('action frénatrice') upon muscular contractions.

While all simple movements show this defect, complex combinations or sequence of movements show another disturbance, *asynergia*. Movements involving trunk and limb muscles, or the muscles of more than one segment of a limb, are decomposed into their component elements, which are carried out in sequence and separately. Synergy, therefore, is the faculty of accomplishing simultaneously the several movements constituting an act. Tremor, or in Babinski's words 'agitation involontaire par oscillations', is a tremor of active muscles and is not seen in repose. It depends upon an imperfect fusion of twitch contractions in the muscle, which Babinski regards as a fundamental defect and calls *discontinuity of movement.*

Adiadokokinesis, the last of the elementary defect symptoms, is a loss of the 'faculty' of executing voluntarily rapidly alternating movements when (and only when) the simple component movements are carried out with normal celerity. Adiadokokinesis depends upon the combined regulating and excitomotor action of the cerebellum which ensures a rapid sequence of contraction to motor impulse.

Cerebellar ataxy is the combined effect of dysmetria, asynergia, discontinuity of movement, and adiadokokinesis.

André-Thomas on the cerebellum. André-Thomas has combined experimental and clinical researches on the cerebellum and appears to have attained a deeper insight into the functions of this organ than other observers. However, the main discrepancies between his conclusions and theirs are largely a matter of nomenclature. This is well seen in his treatment of atonia, which he regards as of rare occurrence, while at the same time he develops a conception of reflex postural tonus far in advance of anything to be found elsewhere in the literature on the cerebellum. According to André-Thomas, muscular hypotonus is rare in cerebellar cases, while asthenia is purely a neighbourhood symptom and not cerebellar in origin. In cerebellar lesions there are grave disturbances of equilibration and also general disorders of motility. The fundamental elements of the latter are dysmetria and discontinuity of movement. As to the characters of *dysmetria* he is in agreement with Babinski, but differs from him in regarding *adiadokokinesis* simply as a natural result of dysmetria and not as a separate defect symptom. As to the cause and significance of *discontinuity of movement* he is in agreement with Luciani. Therefore the function of the cerebellum in voluntary muscular contraction is the exercise of an inhibitory action, as well as an excitomotor action which ensures the fusion of the elementary muscle twitches. In short, the cerebellum regulates muscular contraction. This is, however, a non-specific and secondary function. The main purpose of this organ is to maintain equilibrium, and the most striking result of cerebellar lesions is the loss of the faculty of equilibration. The inability of the cerebellar patient to walk is due to the loss of those tonic muscular reactions by which equilibrium is maintained when the centre of gravity has been displaced. Here we have the true explanation of Babinski's asynergia, which is of course aggravated by dysmetria and discontinuity of movement. Therefore the chief function of the cerebellum is the maintenance, by means of a tonic action on the musculature, of the stability and equilibrium of the body in all movements. When lost, this faculty is imperfectly replaced by voluntary efforts, which lead to an excessive expenditure of energy and result in what Luciani calls asthenia and atonia.

Finally, we come to the most recent clinical study of the cerebellar symptom-complex, that of **Gordon Holmes** (1917), which is based upon the investigation of the acute lesions produced by gunshot wound. Holmes agrees with Luciani that atonia, asthenia, and astasia are fundamental defects of function in cerebellar lesions, but he interprets them somewhat differently from the Italian physiologist, and does not think that they account for all the aspects of cerebellar ataxy. *Atonia* is defined as 'the diminution of that slight constant active tension which is characteristic of normal muscle'. In its absence the muscle is soft to palpation and is unduly extensible. As a result the affected arm hangs inertly at rest, and on movement tends to develop a momentum which causes it to swing beyond the proper range of movement. In this way atonia is a factor in the production of adiadokokinesis. Further, it leads to movement in other segments of the limb, which are not effectively fixed. *Asthenia* is expressed as ready fatigue and as a diminution of the force of movements. The muscles show sudden and unexpected relaxations which impart a jerky character to movements. In addition, there is a reluctance to use the affected arm. Finally, there is delay in initiating, developing, and relaxing the contractions of affected muscles. *Astasia* is closely associated with asthenia, and is due to imperfect fusion of single twitch contractions, so that tremor develops. There are, however, several other elementary factors in the cerebellar symptom-complex. They are decomposition of movement, dysmetria, asynergia, and deviations from the line of movement. *Decomposition of movement* is the same as Babinski's asynergia; while simple movements suffer from the defects we have considered, in complex movements there is a decomposition into the component elements, so that these are carried out separately and in sequence instead of in simultaneous combination. It is 'the result of faulty association in time and degree of the various muscular contractions concerned in an action'. A further result of this is to produce errors in direction of movement. *Asynergia* is 'the absence or disturbance of that proper synergic association in the contraction of muscles which assures that the different components of an act follow in proper sequence, at the proper movement, and are of the proper degree, so that the act is executed accurately and with the least possible expenditure of energy'. Correct adaptation and precision in movement depends upon the accurate functional combination of muscles, and this is lacking in cerebellar lesions. For example, the antagonists or the fixating muscles may come into action before the agonists. Thus a true ataxy, or inco-ordination of movement results. *Dysmetria* means that the range and force of movement is ill-proportioned and is generally excessive (hypermetria). It is due to delayed muscular relaxation which necessarily leads to prolongation of movement beyond the range desired. On the other hand, there may be too little force used, so that the patient undershoots the mark, and for this Holmes, although including it under dysmetria, advances quite a different explanation; namely, that it depends upon a faulty functional combination of muscular contractions. Dysmetria necessarily leads to tremor. *Deviations from the line of movement*: when an arm is raised preparatory to carrying out some purposive movement, it sways aimlessly at first and then starts out for its objective along a zigzag course. The initial unsteadiness is due to defective fixation and is a manifestation of atonia, but the jerky course taken has another origin. It is not due to dysmetria, but to 'disturbance in the regulation of force and sequence of contraction in the different muscles employed'.

The various other disorders of movement seen are combinations of these supposed elementary defect symptoms. Thus adiadokokinesis depends upon atonia, asynergia, dysmetria, and delayed contraction and relaxation.

From this analysis, Holmes concludes that the cerebellum exercises an influence upon the spinal mechanisms concerned in voluntary movement 'by virtue of which these react promptly to cerebral impressions'. It is a motor reinforcing organ, not taking any direct part in the execution of movements, which 'sets' or 'tunes' the activity of certain motor mechanisms so that they respond immediately, effectively, and with appropriate force. Necessarily, the most complex and delicate movements suffer most severely from loss of this influence, and therefore there is no reason to attribute a special equilibrating function to the cerebellum.

On the whole, the general impression derived from the different hypotheses of cerebellar function we have been considering, and from the various analyses of the cerebellar symptom-complex upon which they are based, is that the hypotheses are couched in such vague and general terms as to be little more than restatements of an unsolved problem, while the analyses are diverse and do not reach the fundamental factors of cerebellar ataxy. Dealing with the latter point first, we see that although there is a remarkable agreement as to the facts of observations, yet in the descriptions each symptom has a variety of names, each term is employed in a different sense by the different writers, and all the terms are more or less convertible and vague, so that the reader who attempts to correlate these studies is absolutely bewildered. Perhaps one of the most striking features in all these observations and hypotheses is the non-adoption of the modern conception of muscle tone as a purposive reflex, the meaning of which is posture. The selective incidence of tone in the muscles and its rôle as an essential factor in motor co-ordination have been almost completely ignored. Perhaps an exception should be made in this respect in favour of André-Thomas's conception of a tonic postural activity exercised on the muscles by the cerebellum, the absence of which is the main cause of the disorders following cerebellar lesions. It is true that he does not correlate this loss of postural activity with atonia, but the idea of tonic posture is there. In respect of the other theories, we might make the criticism that they consist simply in translations of symptoms into functions, in a manner which von Monakow has already pointed out to have been one of the most fruitful causes of error and confusion in neurology. For example, because there is excessive movement in cerebellar cases, therefore the cerebellum exercises 'a braking action' on motor innervation, and because there is unsteadiness and fatigability of movement, therefore the cerebellum exerts an excitomotor action on motor innervation. The determination of function in the nervous system is by no means so easy an affair, and theories so based cannot be regarded as serious contributions to the physiology of the cerebellum.

It is to be noted that Luciani's extensive observations have been whittled down in their interpretation into a very general and negative theory of cerebellar functions, which gives us little real insight into the subject. Babinski's theory is frankly of the symptom-translation type, and is therefore equally unsatisfying. Although Holmes has given us one of the most minute studies of the cerebellar symptom-complex, yet his interpretation shows all the characteristics of the earlier studies. Tone is still regarded as a simple matter of 'active tension' in all the muscles, and not as a purposive reflex act. The sudden muscular relaxations which are a manifestation of atonia for Luciani figure here as asthenia and a cause of astasia. Therefore Luciani's three fundamental symptoms become one. The other essential elements in the symptom-complex, as they are defined by Holmes, are impossible to regard as separable and distinct. Rather they appear to be simply particular expressions of a single defect, asynergia. Thus we have seen dysmetria, decomposition of movement, and deviations from the line of movement all defined in terms which are nothing but definitions of asynergia. Conversely, deviation from the line of movement is severally attributed to astasia, decomposition of movement, excessive force of muscular contraction—that is, dysmetria—and is finally dealt with as one of the elementary symptoms. Directly we try to conceive any one of these symptoms apart from the others it becomes clear that they are largely identical. One could not possibly occur without the others also appearing. We are left, therefore, with certain disorders of muscular *contraction* and with asynergia as a disorder of voluntary *movement*. Finally, the theory based upon this analysis is like its predecessors, too general in its terms to reveal the nature of cerebellar functions. When we have admitted that this organ 'sets' or 'tunes' the spinal motor mechanisms so that they respond effectively to cerebral impulses, we are still at the beginning of the problem. What is the nature of this process of setting or tuning? Can it be expressed in exact physiological terms? If not, it does not help us at all.

Leaving aside for the moment all questions of a theoretical nature, let us consider the disorders actually observed. They are as follows:

I. **Abnormalities of the resting muscle.**
  Atonia.

II. **Abnormalities of muscular contraction.**
  (*a*) Slow contraction and relaxation.
  (*b*) Intermittent unsteady contraction.
  (*c*) Disturbances in force of contraction.

III. **Abnormalities of voluntary movement.**
  Faulty functional combination of contraction in the three groups of muscles concerned in a movement; agonists, antagonists, and fixating muscles.

IV. **The effect of voluntary efforts at correction,** which are carried out by a musculature functionally defective in the above senses.

It seems clear that the disorders classified under heading II are of a different order from those under heading III. If muscular contraction in an atonic muscle shows the defects described, then synergy in simple and even more in complex movements cannot possibly be good. Therefore asynergia has still to be interpreted in terms of these underlying disorders, and we have to determine accurately the positive aspect of atonia; that is, the part it plays in the disorders noted under II and III. We see, therefore, that the final and exact analysis of the cerebellar symptom-complex is still to be accomplished. Further, it would seem as though a radical revision and modernization of physiological notions on the part of workers in this field are an essential preliminary to this.

The cerebellum and the labyrinth. So far we have made no mention of the labyrinth, but no complete discussion of the cerebellum is possible apart from a consideration of this important receptor organ of the proprioceptive system. The points of resemblance and of difference between the cerebellar and the labyrinthine symptom-complexes have been discussed by all students of this problem. For the majority of observers there are no essential points of difference in the two groups of symptoms, but for others the distinction is absolute. All consideration of the subject has been coloured by the view, favoured by anatomists and by physiologists alike, that the cerebellum is the central nervous organ of the labyrinth. Sherrington has expressed this most clearly. He has said that the labyrinth is the proprioceptor organ for the head segments of the organism. It is, therefore, the most important receptor of this system. Correspondingly, its central nervous apparatus is extremely complex and receives impulses from all the proprioceptors of the body. It is the 'head ganglion of the proprioceptive system'. Even accepting this view, we should not expect the symptoms of cerebellar and labyrinthine lesions to be identical, for the one is a part of the central nervous system with manifold functional connexions in that system, while the other is simply a peripheral receptor organ. Nevertheless, the two symptom-complexes are very similar in many respects, and are even yet not satisfactorily differentiated. In the paper from which we have quoted, Babinski deals in detail with this question, and it would carry us too far to attempt to discuss it here. But a more general aspect must be considered. Allowing for certain differences in symptomatology, how does the labyrinth influence the motor activities of the organism? That it influences tone and postural adaptation we know from the work of Ewald and from the recent careful studies of Magnus and his collaborators. Luciani and others believe that it does so through its central nervous organ the cerebellum, and that therefore labyrinthine symptoms are in a measure of cerebellar origin. However, Magnus has shown conclusively that the reflex functions of the labyrinths are maintained intact after total extirpation of the cerebellum, and he asserts that *the view which regards the cerebellum as the central nervous organ of the labyrinth is now untenable,* and that in future the functions of the cerebellum must be considered quite apart from those of the labyrinth. He has demonstrated the remarkably complex character of the labyrinthine influence upon muscle tone and postural adaptation. At first sight it might seem as though the cerebellum were bereft of functional significance by these observations, yet no such conclusion is inevitable. Even though complex postural adaptations are possible in the experimental animal deprived of its cerebellum, and even though the reflex paths concerned clearly do not pass through the cerebellum, yet we do not know what part this organ may not play in the intact animal in the integration and control of the various tonic reflexes which go to make up the total posture of the animal under varying circumstances. It may be functionally superimposed upon the postural reflex arcs. An interesting analogy may be obtained when we consider the relation of the cerebral motor cortex to the lower level reflex arcs concerned in the motor taxis of the organism. In the decerebrate animal, perfectly co-ordinated reflex acts are possible, while Magnus and de Kleijn find that in an animal from whom the cerebral hemispheres have been removed, with or without the thalami, not only is standing possible, but when overturned the animal can right itself again. Further, various postures of the body and limbs can be maintained. Nevertheless, this high grade of motor co-ordination is controlled under normal conditions through the medium of the motor cortex and the cortico-spinal path. The functions of the cortex in connexion with co-ordination have already been discussed in *Medical Science,* in an abstract of Sherrington and Leyton's paper on the subject (1920-1, **3**, 349), and we may suppose that the cerebellum occupies a comparable position with regard to the tonic postural reflex activities of the proprioceptive system. This would not interfere with our conception of it as a subconsciously functioning organ, subordinate in its turn to the cerebral hemispheres, and as the head ganglion of the proprioceptive system.

It would explain the persistence of decerebrate rigidity after extirpation of the cerebellum (Sherrington, Magnus, and de Kleijn), and also the profound atonia of acute cerebellar lesions in man.

At the moment it seems as though the problem is rather too complex for the simple resources of the clinician, and necessitates refined methods of analysis such as Sherrington, Magnus, and others have applied with so great a success to the study of the nervous system. When the functions of the labyrinths have been completely defined, we shall have a clearer field for our attack upon the problems of cerebellar function.

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Magnus, R. Welche Teile des Zentralnervensystems müssen für das Zustandekommen der tonischen Hals- und Labyrinthreflexe auf die Körpermuskulatur vorhanden sein? *Arch. f. d. ges. Physiol.*, 1914, **159**, 224.

Magnus, R., und **Kleijn, A. de.** Über die Unabhängigkeit der Labyrinthreflexe vom Kleinhirn und über die Lage der Zentren für die Labyrinthreflexe im Hirnstamm. *Arch. f. d. ges. Physiol.*, 1920, **178**, 124.

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F. M. R. W.

ABSTRACTS

NEUROLOGY

Bramwell, E., and **Dykes, H. B.** **Rib pressure and the brachial plexus.** *Edinb. M. J.*, 1921, **27**, 65.

Sargent, P. **Lesions of the brachial plexus associated with rudimentary ribs.** [**B.**] *Brain*, 1921, **44**, 95.

Pressure symptoms referable to the brachial plexus may be caused by a rudimentary cervical rib or by a rudimentary first thoracic rib (*Medical Science*, 1920, **1**, 630). Sargent recognizes the following types of rudimentary rib: (1) An exaggerated costal process of the seventh cervical rib, not jointed but fused with the transverse process, and continued downwards and forwards as a fibrous band to be attached to the first rib behind the scalene tubercle. (2) A short rib, jointed to the seventh cervical rib by costo-central and costo-transverse joints, and continued onwards as a fibrous band as in Type I. (3) A jointed rib of sufficient length to carry the eighth cervical root on its bony portion, and attached to the first rib by a fibrous band. (4) A jointed rib of which the anterior extremity makes contact with the first rib, the two being fused or united by an irregular articulation. (5) A rudimentary first thoracic rib, the anterior fibrous portion of which is attached to the sternum, usually by a rudimentary costal cartilage. It is important to remember that the first- and last-named types are not always readily apparent in a radiogram. Among the factors determining the onset of symptoms (Bramwell and Dykes), which occur in about 10 per cent. of individuals possessing these abnormalities, are *sex*, females with their drooping shoulder girdles being especially prone to show symptoms; *occupation*, symptoms being relatively often found in clerks, telegraphists, seamstresses, and pianists; *posture*, confinement to bed sometimes brings on pressure symptoms; and, most important, *trauma*. Strains and falls on the shoulder and the lifting of heavy weights are all immediate factors of importance. In both papers, the history of cervical rib from the clinical standpoint and the anatomical factors associated with their occurrences are discussed. Sargent summarizes his observations as follows: Variations in the composition of the brachial plexus are apt to be associated with costal abnormalities, prefixation with a seventh cervical rib, and postfixation with an abnormal first thoracic rib. There is, however, no regular relationship between the costal and neural abnormalities. Of the different types of cervical rib met with clinically, that which most frequently requires operative treatment is represented by abnormally large non-jointed costal process, continued onwards as a fibrous band to be attached as above described.

Symptoms of gradual onset result from continual slight traumatism to the eighth cervical root or lowest cord of the plexus, caused by the tightening of the band during respiration and in certain movements of the arm. With a postfixed plexus symptoms referable to the first thoracic root may be caused by the pressure of a normal first thoracic rib. 'Vascular symptoms' are vasomotor in origin and result from injury to the sympathetic fibres, shortly after their entrance into the eighth cervical and first thoracic roots.

The indications and results of treatment are also discussed. Sargent believes that all the symptoms are capable of relief or cure. In some cases operation is not necessary. A change of occupation, the use of a sling, or muscle-training exercises may be adequate. When these are unavailing, or are not accessible to the patient, operative removal of the rib is called for.

Sargent's paper is accompanied by a series of admirable drawings illustrating the different types of rib in question. F. M. R. W.

Ariëns Kappers, C. U. On structural laws in the nervous system: the principles of neurobiotaxis. [**B.**] *Brain*, 1921, **44**, 125.

The author discusses the factors determining the form, positions, and connexions of the neurones in the fully developed nervous system. That nerve-cells shift during embryonic life has long been known; thus the granule cells of the cerebellar cortex, at first superficial, ultimately take up their position in the deeper layer of the cortex. Kapper's own extensive studies, however, unlike those of his predecessors, which were embryological, have been phylogenetic. The paper may be divided into two parts; that containing the facts of observation, and, secondly, the theoretical considerations based upon them. Kappers has observed the migrations of cells and the outgrowth of cell processes in the brains of various animal species. He believes that the positions taken up and the connexions formed by the neurone are determined by a process of tropism or taxis, which he calls *neurobiotaxis*. The nature of the tropism is bio-electrical, a species of galvano-tropism. By this process are determined the shifting of cells, the formation of selective neurone connexions, and the differences between axone and dendrite—that is, the so-called dynamic polarization of the neurone.

Thus, in sharks, where the dorsal longitudinal bundle is a large and important tract, the abducens nucleus migrates to the dorsal part of the brain-stem, whereas the facial nucleus, which has no functional relation with the dorsal longitudinal bundle, undergoes no such migration. Therefore this process of shifting occurs only between neurone systems which stand in functional relationship, and the factor determining this relationship is what Kapper calls *associated stimulation*. Thus, the dorsal longitudinal bundle is an optic reflex tract, the abducens nucleus is concerned with ocular movements, therefore both are stimulated to activity by visual stimuli. This functional relationship determines the shifting. The cells migrate towards the tract from which they receive most stimuli. In the case of axone connexions a physiological relationship also exists; 'only a functional relationship can cause an axonal relation'. While the cell body and the dendrites are attracted to the source of the stimulus, are stimulo-petal, the axone, on the other hand, grows in the opposite direction, it is stimulo-fugal, or stimulo-concurrent.

Kappers then proceeds in the second part of his paper to discuss a physico-chemical basis of neurobiotaxis. He believes this to be bio-electric.

He quotes the distribution of the dendrites of the Purkinje cells of the cerebellum in the horizontal plane, like the branches of a fruit tree growing against a wall, as a form of distribution which might be expected in an electric field. In the developing nerve-cell, the axone appears before the dendrites, or the Nissl substance. The cell is electro-positive relative to the excited centre from which it receives stimuli, and 'produces a positive offshoot, corresponding to the irradiation of the nervous current from the excitation centre. This cationic offshoot is the axone.' Recently Ingvar has observed the development and outgrowth of an axone in a tissue culture to be determined in direction by an extremely small constant current passed through the culture medium. Later, the dendrites develop, and show a stimulo-petal or cathodo-tropism. This also has been observed by Ingvar in tissue cultures. It is probable that the Nissl substance influences the activity of the dendrites. Kappers further applies this view to explain the existence of a single axone (mono-axonism) and of multiple dendrites (polydendritism), and also for the elucidation of other features of nervous activity. However, as his hypotheses become more speculative, so also they become correspondingly difficult to follow. F. M. R. W.

Greenfield, J. G. On Froin's syndrome, and its relations to allied conditions in the cerebrospinal fluid. [B.] *J. Neurol. u. Psychopathol.*, 1921, **2**, 105.

(1) The syndrome of Froin consists essentially in the approximation of the character of the fluid obtained by lumbar puncture to that of blood plasma. This approximation is never so complete as to render it identical. (2) The change takes place characteristically when the fluid in the lumbar cul-de-sac is completely cut off from communication with the fluid in the ventricles and the cisterna magna, and may be produced by tumours or other disease in the bones of the spine, by tumours of meninges or cord, or by inflammatory adhesions in the pia-arachnoid membrane. (3) The degree of change in the fluid depends more on the completeness of the block than on the nature of the blocking process. But certain constituents of the fluid may vary in relation to the nature of the obstruction. (4) The production of the syndrome is aided by venous congestion below the level of a compression, or by inflammation in the meninges and cord below an area of meningeal adhesion. (5) It is not necessary to postulate any obstruction of the perineural or perivascular lymphatics. The lymph which reaches the subarachnoid space along them aids in the production of the syndrome. Acute peripheral neuritis may in fact itself produce an analogous condition in the cerebrospinal fluid. F. M. R. W.

Gye, W. E. The experimental study of disseminated sclerosis. *Brain*, 1921, **44**, 213.

Gye reviews briefly the experimental work on the pathogenesis of disseminated sclerosis, which was initiated by his own experiments in 1913, when he produced paralysis in rabbits by injections of cerebrospinal fluid from a human case of the disease. More recent observations have confirmed the conclusion then expressed by Gye that disseminated sclerosis is probably caused by an organism. This year, Rothfeld, Freund, and Hornowski (*Medical Science*, 1921, **4**, 347) have thrown some doubt on these positive results, and Gye answers their criticisms. In the present paper he details the results of some experiments in the transmission of the disease in series to animals. A large number of rabbits and of guinea-pigs were inoculated with cerebrospinal fluid from a series of twenty-one cases of the disease in man. All the guinea-pigs were unaffected. Of the rabbits. 17 became ill and paralysed, while 112 remained well or became ill from causes other than the conditions of the experiment. In rabbits which became paralysed the paralysis was not the dominant feature; it was only part of a severe and general illness, which, as a rule, progressed very rapidly. The clinical differences between these cases and those of traumatic haematomyelia from bony injury to the spine seen in rabbits were clear, and there was no possibility of confusion. Gye concludes that disseminated sclerosis is probably an infectious disease, and that the virus may sometimes be found in the cerebrospinal fluid. F. M. R. W.

Birley, J. L., and Dudgeon, L. S. A clinical and experimental contribution to the pathogenesis of disseminated sclerosis. *Brain*, 1921, **44**, 150.

The authors conclude that (1) it is useful to recognize two clinical types of disseminated sclerosis: (*a*) the remittent type characterized by acute exacerbations at widely varying intervals alternating with quiescent periods, and (*b*) the chronic progressive type. (2) In the series investigated (35 cases) the proportion of remittent to chronic progressive cases was as six to one. (3) In early cases of the remittent type, once the acute disturbance has subsided, the patient may present no clinical signs of organic disease over prolonged periods. The possibility of spontaneous cure cannot be denied. (4) In its later stages the remittent type tends to assume the characters of the chronic progressive type. (5) The great bulk of clinical and histological evidence is opposed to the view that these two types correspond to two different pathological processes. On the contrary, they are to be regarded as manifestations of one and the same disease. (6) Cultural and microscopic examination of the cerebrospinal fluid has, in the authors' hands, thrown no light on the pathogenesis of the disease, and no specific organism has been isolated. (7) Attempts to transmit disseminated sclerosis from man to animals (rabbits) have been unsuccessful. (8) The transmissibility of the disease from man to animals they regard as unproved. (9) The evidence in favour of the assumption that a spirochaete is the pathogenic agent is incomplete and in many respects unsatisfactory. (10) The clinical and histological evidence is overwhelmingly in favour of the view that the morbid process underlying the disease is inflammatory in character. F. M. R. W.

Kalberlah, F. Zur Aetiologie und Therapie der multiplen Sklerose. [**On the etiology and treatment of multiple sclerosis.**] *Berl. klin. Wchnschr.*, 1921, **58**, 963.

An earlier paper on this subject by the same author was abstracted in *Medical Science* previously (1920, **1**, 518). Since 1918 Kalberlah has treated thirty-six cases of the disease, acute and chronic, recent and of long standing, with silver-salvarsan alone or combined with quinine-urethane (Merck). He admits that the former is not by any means an ideal drug for the purpose. In one of the series there was apparently complete cure, in some pronounced improvement, in others slight or no amelioration of symptoms. Nevertheless, he is convinced that silver-salvarsan is the most potent agent we possess. As in the cases of such a disease as tabes, treatment must be by repeated courses of injections carried out for an indefinitely long period. His practice is to give bi-weekly injections beginning with a dose of 0·03 gm. and increasing this gradually until a dose of 0·1 gm. is reached. He emphasizes the dangers of larger doses. Such a course of injections may be combined with, or alternate with, a course of intramuscular injections (0·5 gm.) of quinine-urethane, which he regards as a valuable adjuvant. No details are given beyond those reported here, nor are there any clinical case reports.

Kalberlah thinks that it may be safely assumed now that disseminated sclerosis is a disease which can be communicated from man to animals, and is probably a spirochaetosis. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Levaditi, C., Harvier, P., et **Nicolau, S.** Transmission expérimentale du virus de l'encéphalite de la mère au fœtus. [**Experimental transmission of the virus of encephalitis from mother to foetus.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 957.

In this paper the authors describe an experiment in which a pregnant rabbit was inoculated in the anterior chamber with the 'virus fixe' of encephalitis. It died with typical encephalitic lesions on the eleventh day. At autopsy nine foetuses were found and were removed aseptically. The brain and mammary glands of the mother, the placenta, and the brain and liver of one of the foetuses were injected intracerebrally into nine rabbits. With the exception of the liver all the materials used for inoculation were found to contain the virus of encephalitis, although neither the placenta nor the foetal organs presented pathological lesions. W. B.

Harbitz, F. Über die 'Encephalitis lethargica'. [**On lethargic encephalitis.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 458.

Histopathological investigations of the central nervous system from three cases of lethargic encephalitis occurring in Norway during the last months of 1919 and in the first of 1920. The usual lesions characteristic of the disease were found to extend from the cervical enlargement of the spinal cord up to the nucleus of the third cranial nerve. The nervous substance of the upper portion of the floor of the fourth ventricle and round the aqueduct of Sylvius was most affected. The small-celled infiltration was chiefly perivascular in character and formed of large and small lymphocytes and plasma cells. Interstitial foci apparently independent of the perivascular infiltrations were noticed both in the grey and white substances, particularly of midbrain, pons, and medulla oblongata. In comparison with the extent and severity of the inflammatory process the alteration of nerve-cells was found to be very slight. C. d. F.

Luzzatto, A. M., e **Rietti, F.** Contributo all' anatomia patologica dell' encefalite letargica. [**Histopathology of lethargic encephalitis.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 63.

Gamna. C. Contributo allo studio della genesi e del significato dei corpi amilacei. [**On the histogenesis and significance of corpora amylacea.**] *Arch. per le sc. med.*, 1921, **44**, 1.

Favini, V. Contributo allo studio della encefalite epidemica. [**On epidemic encephalitis.**] *Osp. maggiore*, 1921, **9**, 73.

Marcora, F. Sull' origine delle infiltrazioni perivasali nell' encefalomielite epidemica. [**On the origin of perivascular infiltrations in lethargic encephalitis.**] *Hæmatologica*, 1921, **2**, 323.

Pecori, G. L'encefalite epidemica a Roma. [**Epidemic encephalitis in Rome.**] *Ann. d'ig.*, 1921, **31**, 32.

Reference has already been made to the investigations of Luzzatto and Rietti (*Medical Science*, 1921, **3**, 366) who now publish a much longer paper on the subject. In this they discuss their findings and compare them with those of other authors. Nothing new, however, is added either to the description given in their previous note or to what we already know on the histopathology of lethargic encephalitis. In the concluding pages the authors show by means of comparative considerations that the lesions observed in acute and subacute cases of the malady are sufficiently characteristic to render rather difficult a confusion with other inflammatory processes of the central nervous system such as polyomyelitis, trypanosomiasis, Borna disease of horses, severe acute and chronic progressive chorea, nervous influenza. All these forms have many points of analogy both with lethargic encephalitis and one with the other. But there are also differences which appear sufficient for discriminative purposes, at least in most cases.

Gamna has made use of the material previously employed for his research on lethargic encephalitis to which reference has also been made (*Medical Science*, 1921, **4**, 452). From the observations made from that and other material freshly investigated, he comes to the conclusion that corpora amylacea frequently occur in the central nervous system from cases of lethargic encephalitis, and that they originate from degenerative products of nerve-cells and nerve-fibres, which, fluid at first, solidify in course of time within the interstices of the nervous substance.

Favini has been able to investigate histopathologically two cases of lethargic encephalitis out of 39 clinical observations. He is of the opinion that 'the morbid findings are identical with those of any myelo-meningo-encephalitis of toxi-infectious origin, and that they are not characteristic enough for a differentiation between them and those of many other acute and sub-acute inflammatory processes of the central nervous system'. In one of the two cases histologically investigated, the inflammatory and infiltrative changes were diffused over the whole of the spinal cord, nerve roots, and optic nerve. This finding might have been of great interest had not the patient contracted syphilis one year before.

Marcora's investigations have been carried out in five cases of lethargic encephalitis in which death occurred between the eighth and sixteenth day from the onset of symptoms. The changes observed were those typical of relatively acute cases of the disease. As to the perivascular infiltrations, to which special attention was paid by the author, he is of the opinion that most of the cells out of which they are formed originate from a proliferation and transformation of 'perivascular connective tissue elements'. Indeed, modern views attribute to them an embryonic character and a very active part in the production of the so-called small-celled infiltrations characteristic of productive inflammatory processes. This applies chiefly to the plasma-cells and offers elements probably belonging to Maximow's group of 'wandering cells at rest'. As to the small round cells, morphologically identical with the lymphocytes of the circulating blood, the question of their origin must be left in abeyance for the time being, because it is not possible to exclude, in a definite way, that they may, at least in part, migrate from the blood-stream into the nervous tissue.

Interesting epidemiological considerations on lethargic encephalitis in Rome are contributed by Pecori. A few cases were observed during the first months of 1919, but this small epidemic passed almost unobserved since only about a dozen people were apparently affected. A few sporadic cases also occurred, probably during the summer of 1919, but a true epidemic only began in November of the same year and lasted till the end of February of 1920, though sporadic cases continued to be observed in the following months. It is worth noting that this epidemic was preceded and accompanied by a relatively great number of cases of hiccough. This generally lasted three or four days and was accompanied, in a limited number of instances, by slight fever and gastric disturbances. In most cases, recovery promptly followed; in some it gave place to a typical form of lethargic encephalitis. The author is therefore of the opinion that epidemic hiccough is nothing else than a mild form of the malady. The total number of ascertained cases observed in Rome between November 1919 and August 1920 was 338; of these 158 were male and 180 female. The maximum of incidence and mortality in regard to age was between 21 and 40. The greatest mortality was observed amongst workmen and Jews. Most cases had been previously affected by influenza; but the author attaches little importance to this observation because only a few people were not affected by influenza in Rome during the winter of 1918–19, and all one can safely say, from an epidemiological point of view, is that influenza does not confer any immunity against lethargic encephalitis. The malady prevailed in the poorer quarters of the town which in Rome are also most crowded and often dirty. As to the clinical types of the disease the stuporous and hyperkinetic ones were most frequent. The greatest mortality was observed in the erethistic, stuporous, and mixed forms. As to the contagiousness, the observations of Pecori are similar to those made in other countries, and he comes to the conclusion that propagation of the malady from one to another individual can be explained in most cases only by assuming the existence of healthy or slightly affected carriers. C. d. F.

Rapisarda, G. Le miscele siero-tubercoliniche nella tubercolosi sperimentale della cavia. [**Influence of sero-tuberculinic mixtures on experimental tuberculosis of guinea-pigs.**] *Ann. d'ig.*, 1921, **31**, 90.

The fatal course of experimental tuberculosis in guinea-pigs does not appear to be influenced in any way by a treatment with increasing doses of pure human tuberculin. The same animals when treated with increasing doses of mixtures of human tuberculin and guinea-pig's serum constantly show: (1) an amelioration of the local lesion and general conditions; (2) an increase in weight; (3) a prolonged resistance to the infection. C. d. F.

Pupilli, G. Sul valore etiologico del *Proteus vulgaris* nel cholera infantum. [**On *Proteus vulgaris* as an etiological factor of cholera infantum.**] *Ann. d'ig.*, 1920, **30**, 763.

Experiments were made on very young laboratory animals such as rabbits, guinea-pigs, and puppies to which varying doses of pure cultures of *Proteus vulgaris* were administered *per os*. The results did not confirm those obtained by Metchnikoff in similar experimental conditions, since in the author's opinion the morbid changes thus caused have very little likeness to the symptomatology of cholera infantum. The same happened when the pathogenic action of *P. vulgaris* was favoured by an abnormal state of the enteric tract experimentally caused by various means. Small laboratory animals and particularly very young rabbits may die after the ingestion of large, and sometimes even small doses of proteus cultures, but this seems to be due to a toxic action of the germ, and does not prove that it is the direct aetiological factor of cholera infantum. However, *P. vulgaris* may play a certain rôle in the pathogenesis of the disease as in any other enteric affection favourable to its development. C. d. F.

Binda, P., and **Perin, A.** Contributo allo studio della proprietà indoligena di alcuni terreni culturali. [**On the indologenous property of certain culture media.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 213.

By means of a strain of *B. coli communis*, not indologenous in ordinary culture media, the authors were able to make various observations which they summarize as follows: (1) The presence of free or combined tryptophan (indolalanin) in culture media is necessary and sufficient to obtain a production of indol. (2) Tryptophanized culture media are the most delicate means of study of the indologenous property of micro-organisms. (3) The reactions with glyoxylic acid and bromine water are quite suitable to test the indologenous property of culture media. (4) Tryptophanized water is by itself sufficient for the development of certain germs.

C. d. F.

Pergola, M. Valore dell' arbutina nell' identificazione dei vibrioni. [**Use of arbutin for the identification of vibrios.**] *Ann. d'ig.*, 1921, **31**, 265.

The arbutin reaction may have a certain value for the identification of cholera and other vibrios. The former generally break up arbutin into glucose and hydroquinone in a rather sluggish way, while the latter either have a practically negative effect or decompose the glucoside very actively and rapidly. C. d. F.

Cowie, D. M., and **Kempton, R. M. Studies on the nature of the action of non-specific protein in disease processes. I. Typhoid protein (dead typhoid bacilli) and soluble toxin.** *J. Med. Research*, 1921, **42**, 227.

This is a study of the action of dead typhoid bacilli on diphtheria toxin. When allowed to remain in intimate contact with diphtheria toxin at 37° C. for one hour dead typhoid bacilli had left the toxin unaffected. Dead typhoid bacilli injected subcutaneously or intravenously do not protect guinea-pigs against 1 M.L.D. of diphtheria toxin. On the other hand, normal horse serum injected subcutaneously at the same time as a fatal dose of toxin protects the guinea-pig perfectly. W. B.

Cowie, D. M., and **Greenthal, R. M. Studies on the nature of the action of non-specific protein in disease processes. II. Horse serum and soluble toxin.** *J. Med. Research*, 1921, **42**, 261.

The authors found that 1 c.cm. of normal horse serum when injected subcutaneously or intravenously into guinea-pigs simultaneously with diphtheria toxin will always protect against 1 and may protect against as many as 8 lethal doses of toxin. Larger doses of serum will protect against larger doses of toxin, but the effect is not necessarily proportional. By precipitating normal horse serum with alcohol it was found that the protective property resides in the protein portion and not in the alcohol-soluble extract. By similar treatment of diphtheria antitoxin the authors considered that the antitoxin factor is destroyed by the alcohol. As some of the so-called 'normal horse serum' on the market is taken from horses which have been previously injected with toxins or other antigens it may be stated that the normal horse serum used by the authors was obtained from a horse in which this history could be definitely excluded. W. B.

Gulino, M. Comportamento della siero-agglutinazione specifica verso il tifo e delle relative siero-agglutinazioni di gruppo in rapporto ad influenze diverse di natura fisica e chimica. [**Influence of various substances on agglutination test.**] *Ann. d'ig.*, 1921, **31**, 160.

The specific and group agglutinating power of antityphoid sera is greatly influenced and may even disappear in consequence of various treatments such as addition to the serum of concentrated solution of NaCl (1·5 – 2 per cent.); warming of the serum at temperatures varying between 56° C. and 75° C. for one or two hours; contact of the serum with bacterial suspensions or with kaolin powder; addition to the serum of alkalis and acids. C. d. F.

Taniguchi, T. Studies on heterophile antigen and antibody. [**B.**] *J. Path. & Bacteriol.*, 1921, **24**, 217.

Ten years ago Forssmann of Lund showed that the injection of emulsions of organs of certain animals into rabbits induces the formation of immune body for sheep's blood corpuscles. Owing to the fact that the sheep blood haemolysin thus generated differs from that obtained, in the usual way by injecting sheep corpuscles into the rabbit, it has been called 'heterophile' in contradistinction to 'isophile', and the tissues which can evoke the formation of heterophile antibodies are called 'heterophile (heterogenic) antigens'. The organs of the guinea-pig, horse, dog, cat, mouse, fowl, and tortoise function as heterophile antigens, whereas the organs of man, rabbit, ox, sheep (except blood corpuscles), rat, goose, pigeon, frog, &c., are devoid of this property. The present author has given a lucid analysis of the complicated literature associated with the subsequent developments of these heterophile antigens and antibodies, and suggests that instead of the terms heterogenous, heterogenic, or heterophile, it is preferable to use the names Forssmann's antigen and antibody since the important fact is not that the antibody is generated by a different kind of antigen, but that it is an affinity for the receptors of a species other than those in response to which it was developed. The present research deals with (1) the specific fixation of heterophile antibody by the lipoids of heterophile organs; (2) complement fixation exhibited by heterophile antibody in the presence of alcoholic extracts of heterophile antigens; (3) precipitation of emulsions of lipoids derived from heterophile tissues by heterophile antibody; (4) constituents of alcoholic extracts with which heterophile receptors are associated; (5) the question whether lipoids of heterophile tissues are capable of generating heterophile immune body. For those who are especially interested the paper must be read in the original. Among other points of importance the author points out that heterophile (Forssmann) antigen is not equally distributed in different organs of the same species, for in the case of the guinea-pig, the kidney is richer in antigen content than the liver, whereas brain and serum contain but small amounts. The receptors of heterophile antigens reside in the lipoids of the tissues, especially in those which are soluble in alcohol and ether but insoluble in acetone, the so-called lecithin fraction. Lipoids of other tissues do not react with heterophile antibody. Forssmann haemolytic antibodies exhibit three other characteristic reactions: (*a*) they combine with lipoids derived from heterophile antigens; (*b*) they fix complement in the presence of such antigens; (*c*) they form precipitates with emulsions of lipoids. In a quantitative sense the haemolytic power of such an antiserum is always parallel with its precipitating and complement-fixation properties. The property possessed by rabbit serum of fixing complement along with lipoids of heterophile antigens is distinct from that of reacting with the lipoids of other tissues so as to yield a positive Wassermann reaction. Specific heterophile reactions are intensified by the addition of cholesterol to the solution of lipoids, and also by increasing the turbidity of the emulsion. The power to react specifically with heterophile antibody *in vitro* and the capacity for developing the antibody *in vivo* are markedly independent properties. For example, the alcohol-soluble lipoids are practically devoid of the ability to evoke the generation of heterophile antibody. Neither does the protein residue, remaining after the extraction of the lipoids, act as an antigen. The author believes that the antigenic power lies in some lipoid-protein complex, whereas the combining affinity resides in the lipoids.

W. B.

Dervieux, M. Procédé de diagnostic individuel du sang et du sperme. [**Method for determining the individual sources of blood and semen.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1384.

Dervieux finds that the blood-serum of a rabbit immunized against human semen gives rise to precipitins when brought into contact with both human blood and semen, whilst if the animal is immunized against human blood the precipitin reaction will be obtained with human blood only.

After studying these reactions under various conditions Dervieux comes to the conclusion that by using the serum of a rabbit immunized against human semen it is possible:

(1) to determine the human origin of a specimen of semen;

(2) to state that a sample of semen comes from one particular individual, and not from another;

(3) to determine the human origin of a sample of blood;

(4) to determine the sex of the individual who supplied a specimen of blood;

(5) to state that a sample of blood comes from some particular individual.

J. R. P.

Hirsch, E. F. Changes in the alkali reserve, sugar concentration and leucocytes of the blood in experimental infections. *J. Infect. Dis.*, 1921, **29**, 40.

In previous work the author showed that after intravenous injections of living cultures of pathogenic bacteria there was a leucopenia and a diminution of the alkali reserve of the whole blood, within two hours. Subsequently the leucocytes appear in increased numbers and the alkali reserve returns to or exceeds its original level. In the present paper the author has continued this line of research and has estimated in addition the effect on blood sugar concentration of intravenous injection of living cultures of various members of the typhoid-paratyphoid-dysentery-coli group of bacteria, *S. haemolyticus*, *Pneumococcus*, and *B. welchii*. The determinations of alkali reserve, sugar concentration, and number of leucocytes were made before and at intervals after the injection of bacteria, the results being set out in tabular form. Depression of the alkali reserve in rabbits following intravenous inoculation of cultures of the above-mentioned bacteria is accompanied by a transient hyperglycaemia, the degree of the latter depending, apparently, on the extent of the alkali reserve diminution. Subcutaneous administration of sodium carbonate or bicarbonate solutions does not prevent the acidosis produced by the bacterial injections. The injection of acid potassium phosphate depresses the alkali reserve of the blood, and with this there is an increase in the concentration of sugar in the blood similar to that produced by the injections of bacteria. The changes in the leucocytes are also similar. The concentration of sugar in the blood appears to be independent of the leucopenia and subsequent leucocytosis. W. B.

Price-Jones, C. The sizes of red blood cells in emphysema. *J. Path. & Bacteriol.*, 1921, **24**, 326.

The author in continuing his previous methods of investigation (*Medical Science*, 1921, **4**, 366) deals here with the sizes of red blood cells in a series of 22 cases diagnosed as emphysema. The ages of the patients varied between 35 and 100. Twenty healthy persons at ages ranging from 19 to 90 were examined as controls. The result showed that the red blood-corpuscles of emphysematous persons are larger than those in health. The average red cell diameters ranging from 7·33 μ to 8·17 μ with a mean diameter value for the 22 cases being 7·69 μ. The average red cell diameters in the healthy ranged from 6·96 μ to 7·48 μ, the mean diameter being 7·24 μ. The difference (0·45 μ) between the average diameters in the two classes is regarded by the author as 'significant', and he considers that the increased size of the erythrocyte in emphysema is probably associated with an increased quantity of CO_2 in the blood in spite of normal reaction. He thinks that CO_2 must have a special swelling action on the red cells out of proportion to its acidity. W. B.

Veratti, E., e Cattaneo, D. Sull' infezione sperimentale da paratifo B nel coniglio. [**On experimental infection of rabbit with *B. paratyphosus* B [B.].**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 255.

Besredka (*Ann. de l'Inst. Pasteur*, 1919, **33**, 557 and 882; *Bull. de l'Inst. Pasteur*, 1920, **18**, 121) has recently shown that the administration *per os* of a certain quantity of ox bile to rabbits renders them very sensitive to infection with *B. typhosus* or *paratyphosus*. Besredka explained this fact by assuming that the bile had a desquamative action on the mucous membrane of the small intestine, thus preparing it for a vigorous development of the germs inoculated into the animals either *per os* or intravenously. Veratti and Cattaneo have repeated Besredka's experiments by means of cultures of *B. paratyphosus* B, and found that the bile, while really having the sensitizing effect observed by Besredka, has no desquamative action of any sort. In fact no histological lesions of the mucous membrane of the small intestine could be observed, even after the introduction of large quantities of ox bile into the stomach of rabbits by means of a gastric tube. On the other hand, the sensitizing effect of bile could be obtained also by means of repeated injections of the same into the subcutaneous tissue. The influence of bile upon rabbits in regard to the infection with *B. typhosus* and *paratyphosus* must, therefore, be considered as due not to a local but to a general action on the whole organism. C. d. F.

Leone, R. Contributo alla diagnosi microbiologica della dissenteria amebica. [**On micro-biological diagnosis of amoebic dysentery.**] *Riforma med.*, 1921, **37**, 129.

For the rapid recognition of the amoeboid forms of *Entamoeba histolytica* the best method was found to be that proposed by Cutler and Williamson (*J. Path. & Bacteriol.* 1916–17, **21**, 511). This consists in the employment of a freshly prepared 1 : 10,000 solution of neutral red in 0·85 per cent. NaCl. A loopful of faeces is emulsified in a drop of the staining solution on a glass side. The preparation is covered with a cover-slip and examined under an ordinary high power objective. A warm stage is an advantage but is not essential. In such a preparation the vegetative forms of *E. histolytica* take up the neutral red, and the stained amoebae can be readily seen. The pink dye is uniformly distributed throughout the endoplasm. According to Cutler and Williamson the ectoplasm remains unstained; Leone noticed that it was often coloured a pale yellow. *E. coli*, *Cercomonas hominis* and *intestinalis* are not stained and easily recognized by their greyish colour. Cysts of *E. histolytica* appear as colourless refractile bodies. According to Cutler and Williamson, *Chilomastix mesnili* is affected by neutral red when in the active condition, the bodies of the vacuoles in the endoplasm appearing pink. Instead of neutral red, Magdala red can be employed but the results are not so constant.

To start cultures of *E. histolytica*, Leone recommends the use of the slightly alkaline peptone water of Nocht in test-tubes to each of which 2 c.cm. of a freshly prepared 1 : 2,000 solution of neutral red in 0·75 per cent. of NaCl are added after sterilization. Five or six loopfuls of the suspected faeces are inoculated into the tubes and these kept in an incubator at from 30° C. up to 37° C. for about seven hours. After this time, if the amoebae were present in the faeces they will have multiplied and become stained by the neutral red, so that their recognition does not present any difficulty. For subcultures it is advisable to have resort to the egg medium of Dean and Mouat (*J. Roy. Army Med. Corps* 1916, **26**, 189 and 349) to which a few drops of human blood are added as originally proposed by Cutler (*J. Path. & Bacteriol.* 1918, **22**, 22). C. d. F.

Ninni, C. (1). Modifica al metodo di Kitasato per l'isolamento del B. del tetano. [**Modification of Kitasato's method for the isolation of *B. tetani*.**] *Ann. d'ig.*, 1920, **30**, 684.

Ninni, C. (2). La presenza del bacillo del tetano nel tubo digerente dei piccoli erbivori e sua tossicità. Ricerche sperimentali sul tetano coltivato in simbiosi. [**On the presence of *B. tetani* in the gastro-enteric tube of small laboratory animals. Experiments on *B. tetani* grown in symbiosis with other germs.**] *Ann. d'ig.*, 1920, **30**, 756.

Ninni, C. (3). Esaltazione della tossicità dei bacilli del tetano. Tetano cronico delle cavie. [**Increase in the toxicity of *B. tetani*. Chronic tetanus of guinea-pigs.**] *Ann. d'ig.*, 1921, **31**, 58.

Ninni, C. (4). Azione della bile sulla tossina del tetano. [**Action of bile on tetanus toxin.**] *Ann. d'ig.*, 1921, **31**, 121.

To isolate the *B. tetani* it is not necessary to heat the suspected material to 80° C. for five minutes as originally proposed by Kitasato. Heating at 60° C. for an hour is ample for the purpose with the advantage of not altering the toxicity of *B. tetani*. Working with this and other methods Ninni found that *B. tetani* can be constantly isolated from the various portions of the digestive tract of rabbits and guinea-pigs. The *B. tetani* thus isolated is always toxic, though the degree of toxicity may vary. Pure cultures, preferably in liver broth, are necessary to form a right opinion of the toxicity of *B. tetani* isolated from the dejecta of domestic animals. Experiments made with *B. tetani* grown in culture media with *B. bulgaricus*, *B. coli communis*, *Streptococcus*, and other germs show that the biologic activity of *B. tetani* can be modified by antagonistic germs, and thus its virulence be reduced or increased. In Ninni's experiments the greatest attenuating action was displayed by *B. bulgaricus*, *B. acidi lactici*, while *Enterococcus* had an opposite effect.

The toxicity of *B. tetani* may also be attenuated or increased by varying the organs with which the broth for its cultures is prepared. Thus, in comparison with liver broth, generally used for keeping the toxin of *B. tetani*, spleen broth attenuates its virulence from 5 to 10 times, adrenal broth from 50 to 100 times. On the other hand, brain increases its virulence from 5 to 10 times, kidney about 50 times; heart about 500 times. The effect of pancreas is the same as that of liver in regard to the minimum lethal dose, which remains the same in both cases. But guinea-pigs inoculated with doses of cultures in pancreas broth from 100 to 1,000 times smaller than the minimum fatal one become affected by a form of chronic tetanus characterized by fall of the hair and enlargement of the spleen, which requires further investigation.

To study the action of bile on tetanus, experiments were made with: (1) fresh bile of guinea-pigs; (2) eight days old bile; (3) old bile and fresh serum of guinea-pigs; (4) bile warmed for half an hour at 56° C.; (5) warmed bile and fresh guinea-pig serum; (6) taurocholic and glycocholic acids diluted in the proportions in which they are found in human bile. It was found that only fresh bile has a neutralizing effect on tetanus toxin, this being probably due to enzymes which cease to be active under the influence of time, heat or other treatment. From these results the author draws the conclusion that tetanus toxin is very likely of the nature of a lipoid. This agrees with the knowledge that bile emulsifies fat and that tetanus toxin chiefly affects the central nervous system. Moreover it explains why the virulence of *B. tetani* is increased by culture media prepared with organs rich in lipoids, such as brain and heart.

C. d. F.

Bompiani, G. Osservazioni istopatologiche sulla roseola del tifo esantematico. [**Histopathological observations on the rash in typhus.**] *Arch. per le sc. med.*, 1920, **43**, 167.

The author is of the opinion that Fraenkel's nodules constitute a characteristic lesion of the skin in typhus, and that a diagnostic value may consequently be attributed to them when observed together with the clinical symptoms of the disease. During the critical period of the malady, in addition to the nodules, diffuse small-celled infiltrations can be observed in the skin. These consist of: (1) lymphocytes; (2) large mononuclear cells of the epithelioid type; (3) fusiform cells similar to fibroblasts; (4) plasma cells; (5) nuclei smaller than those of ordinary lymphocytes (Fraenkel's nuclei); (6) a few cells of an uncertain type characterized by a well stained nucleus and a homogeneous eosinophil cytoplasm; (7) a few polymorphocytes. These various elements are generally mixed together in changing proportions. In more advanced stages of the disease (22nd to 27th day) lymphoid and fibrous nodules can be seen, which the author is inclined to consider as due to the healing up of Fraenkel's nodules. Where such nodules and diffuse small-celled infiltrations are noticed, a very fine network of connective tissue fibres can be observed, which appear to be of the same nature as the so-called reticular tissue. In about the same places the elastic fibres of the corium seem to undergo degeneration and to disappear. C. d. F.

D'Agata, G. Necrobiosi putrida gassosa. [**Putrid gaseous necrobiosis.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 119.

The author has been able to isolate from a human case of emphysematous gangrene a sporogenous anaerobic germ which, because of its gasogenous and putrefying properties and other biological characteristics, could be considered as similar to, if not identical with, Metchnikoff's *B. sporogenes.* The germ, when inoculated intramuscularly into animals (guinea-pigs), gave origin to a histopathological condition which the author proposes to term 'putrid gaseous necrobiosis'. This was characterized by a process of dissociation and vacuolization of the muscle fibres which, in a more advanced stage, underwent liquefaction and complete disruption. At the boundaries between affected and healthy muscular tissue, a zone of small-celled infiltration could be seen. After some months the isolated germ had lost part of its virulence, but this could be restored either by mixing it with a 'microbic toxin' from *B. perfringens,* or by having resort to the method of Bullock and Cramer (injection of 0·5 c.cm. of a 10 per cent. solution of calcium chloride). C. d. F.

Van Gehuchten, P. Les organes à sécrétion interne dans la gangrène gazeuse expérimentale. [**The ductless glands in experimental gas gangrene.**] *Ann. de l'Inst. Pasteur,* 1921, **35**, 396.

At the suggestion of M. Weinberg the author has carried out histological and histochemical studies on the ductless glands, especially the

adrenals of 65 guinea-pigs which had been inoculated with pure cultures of pathogenic anaerobes, with mixed cultures of anaerobes, and with mixed cultures of anaerobes and aerobes, particularly *B. proteus*. Whereas the changes in the thyroid and pituitary glands were relatively slight, the adrenals were found to be severely affected. In the cortex there was a marked disappearance of fatty substances from the spongy layer, cholesterin disappearing within 48 hours. Neutral fats disappeared more slowly. The author brings forward evidence that cholesterin may be produced by the adrenals. In the medulla the chromaffin content of the cells diminishes and the cells themselves degenerate. In cases that survive long enough for reparative changes to ensue the histological and histochemical changes above described are not so marked. The use of polarized light was employed with great advantage in interpreting the changes found.
W. B.

Ficai, G. Reperto di corpuscoli nel tifo esantematico. [**Minute bodies in typhus.**] *Ann. d'ig.*, 1920, **30**, 733.

As briefly described in a preliminary note on the same subject (*Policlin.*, 1920, **27**, 133), peculiar bodies were at first observed by the author in the epithelial cells lining the mucous membrane of the stomach of lice found on typhus patients, but not in lice obtained from other sources. These bodies were of two forms: very small (2μ in diameter) with homogeneous structure, and larger ones (4 to 6μ in diameter) containing either four to five secondary corpuscles or a single central body or nucleus. The same bodies were afterwards found by Ficai also within and without the nerve-cells of pieces of brain obtained from cases of typhus.

The bodies stain well with diluted Giemsa, Unna's polychrome methylene blue, Ehrlich-Pappenheim's triacid mixture, toluidine blue, and thionine, but the author particularly recommends staining paraffin sections first for 2 to 3 hours in diluted May-Grünwald mixture (1 : 5), and then for 24 hours in diluted Giemsa's stain (1 : 20), changing this once if too much precipitation is formed. Lice are best fixed in the usual mixture of acetic alcohol-corrosive sublimate. Pieces of the brain used by the author had been already hardened in 10 per cent. formalin, alcohol, and Müller's fluid. In the case of the latter he found it useful to re-transfer them into 10 per cent. formalin for a time sufficient to extract all the bichromate.

Ficai's bodies have a remarkable morphological analogy with those observed by Kleine and Schiffmann, Borrel and Paschen, Negri, Sinigaglia, Casagrandi, Volpino, Prowazek, Da Fano, Levaditi, in other diseases the cause of which appears to be a filter-passing virus. C. d. F.

Stevenson, A. C., and **Balfour, A. Notes on the histopathology of typhus fever.** [**B.**] *J. Path. & Bacteriol.*, 1921, **24**, 289.

This paper deals with an exhaustive examination of the tissues of 5 cases of typhus fever, four of which were stated to be uncomplicated instances of the disease, the remaining case being complicated with pneumonia. The special object of the investigation was to compare the histological findings with the descriptions given in the literature, and in particular to see if any appearances resembling those which have been regarded as Rickettsia bodies could be seen. The present authors confirm in the main the pathological lesions described by Eugene Fraenkel, Aschoff, Herzog, and many others, and they give a lucid picture of the microscopic changes to be found in persons dead of typhus. They are not, however, convinced of the possibility of differentiating the so-called Rickettsia bodies from other granules of diverse kinds which may be met with in the lesions. They advocate the adoption of what they call an 'Asquithian' ('Wait and see'?) attitude until further investigations throw more light on the question. W. B.

Marinesco, G., et **Craciun, E.** Lésions du système nerveux dans le typhus exanthématique et leur rapport avec la névrite ascendante. [**Lesions of the nervous system in typhus.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1258.

The authors find that in severe fatal cases of typhus the whole of the central nervous system as well as the peripheral nerves show the inflammatory lesions of the disease, and they give a minute description of these lesions which they trace from the peripheral nerves through the posterior root ganglia into the spinal cord.

They conclude from their studies that in addition to the blood acting as a path of infection, as shown by Charles Nicolle, the lymphatics of the peripheral nerves can also carry the virus into the central nervous system. J. R. P.

Weil, E., und **Felix, A.** Ueber die Beziehungen der Fleckfieberagglutination zum Fleckfiebererreger. [**On the relation of typhus agglutination to typhus virus.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **31**, 457.

This is an extensive research dealing with the Weil-Felix reaction in relation to the virus of typhus fever. According to the authors, the sera of rabbits infected intraperitoneally or subcutaneously with the cerebral substance of typhus guinea-pigs constantly agglutinate cultures of *Proteus* X 19. The cerebral substance of normal guinea-pigs has not this effect. On emulsions of various bacteria (*Proteus vulgaris, B. coli, B. dysenteriae, M. melitensis, &c.*) which have been said to give the Weil-Felix reaction with the sera of typhus patients, the sera of rabbits inoculated as above has no effect. No agglutinins are developed in the rabbit if the typhus virus is heated to 58° C. for half an hour. Agglutinins for *Proteus* X 19 are developed in the rabbit after such small doses as 0·001 (gm.?) of infected guinea-pig brain. By means of the agglutinating action of rabbits' serum it can be shown that the typhus virus exists in the guinea-pig brain 5 days after the apyrexia following the injection has taken place. If typhus virus is kept at a low temperature for 48 hours the inoculation of the brain of guinea-pigs which have received such virus, produces only inconstant Weil-Felix reactions in the sera of rabbits. W. B.

Herxheimer, G., und **Gerlach, W.** Über Leberatrophie und ihr Verhältniss zu Syphilis u. Salvarsan. [**On atrophy of liver in relation to syphilis and salvarsan.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 93.

Detailed account of the pathological findings on six young adults who had been treated for early syphilis (see *Medical Science*, 1920, **3**, 266). In the present paper the authors fully describe the changes observed in their six cases and also discuss the question of the regenerative changes noticeable in the liver in cases of subacute atrophy. In regard to this point they come to the conclusion that such changes are due in part to a compensatory and hyperplastic proliferation, in part to a true regeneration of the surviving cells of the liver. A connexion between these regenerative processes and regeneration of the bile-ducts, as admitted by some authors, should be excluded. Proliferative phenomena on the part of the bile-ducts can be easily observed in all cases of subacute atrophy, but a direct transformation of the epithelium of the newly-formed bile-ducts into liver cells was not seen and appears highly improbable. C. d. F.

Stoeckenius, W. Beobachtungen an Todesfällen bei frischer Syphilis. [**Observations on fatal cases of recent syphilis.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 185.

The author has had the rare opportunity of thoroughly investigating four fatal cases of recently contracted syphilis. All of them (a girl of 20 years of age and three young men) were affected with declared syphilis in its second stage, and suffering in addition from a salvarsan dermatitis. One of them committed suicide, while the other three apparently died of acute salvarsan intoxication. At the post-mortem examination of the girl (Case I) a chronic peribronchial lung tuberculosis with fresh disseminations in the spleen, kidneys, and heart-muscle, was at first suspected; but after a more minute investigation this supposition was dropped and the alterations ascribed to acute syphilis. In the second case the author also thought at first of a nodular caseous form of tuberculosis of the suprarenal glands; but neither tubercle bacilli nor Much's granules could be detected in such organs, and no trace of a decided tuberculous process was found in any other organ. The third case was likewise mistaken for a primary tuberculosis of the mesenteric lymph glands, with secondary nodules in the spleen, kidney, and other lymph glands. Only in the fourth case tuberculosis was excluded from the beginning, chiefly because of the absence of a primary localization from which the apparently secondary dissemination in various organs might have taken place. In addition, the minute foci found in the spleen, lymph glands, and small and large intestine had a peculiar blunt aspect and a grey-whitish colour, unlike the shining aspect of recent miliary tubercles.

Histologically all these various lesions presented the common picture of granulomata with a varying amount of necrosis and connective tissue proliferation, so that the microscopic discrimination between tuberculosis and syphilis was likewise surrounded by many difficulties. Chief amongst them was the negative result by which the search for both tubercle bacilli and spirochaetes had been attended. The histopathological diagnosis had, therefore, to be based on the results of a purely microscopic investigation. In this connexion due weight was given: (1) to the proliferation of the connective tissue around and within the focal lesions; (2) to the existence of a varying degree of exudative and infiltrative changes in the sustaining framework of various organs; (3) to the alterations of blood-vessels. As to 1 the author recalls the fact that a proliferation of connective tissue is generally observed also round tuberculous lesions, when showing a tendency to recovery, and that Virchow himself has emphasized the importance of the prevailing affection of the connective tissue for the recognition of alterations, almost characteristic of the so-called tertiary syphilis. The same applies to the second point and to the fact that the parenchymatous alterations were either inconspicuous or evidently secondary to those of the sustaining framework. As to the alterations of the blood-vessels, the author points out that they were widespread and of a rather changing character. Most affected were the pre-capillaries (arteries and veins), in the external and middle coats of which chiefly infiltrative and proliferative changes could be seen. A swelling of the endothelium of the smallest blood-vessels was also noticed; but as a rule the intima was the least affected. An exception to this was found in the blood-vessels of the intestinal walls in Case IV, where severe proliferative changes had resulted in thromboses of various degrees. In spite of all this, had the author not known for certain that his cases were affected by a severe form of syphilis, it might have been much more difficult, and perhaps impossible, to exclude tuberculosis in a decided manner. And this is perhaps the most instructive of his interesting observations. C. d. F.

Klarenbeek, A. (1). Experimentelle Untersuchungen mit einer beim Kaninchen spontan vorkommenden und dem *Treponema pallidum* ähnlichen Spirochäte. [**Experimental researches with a spirochaete oocurring spontaneously in the rabbit and resembling *Treponema pallidum*.**] *Centralbl. f. Bakteriol.* (&c.), 1921, Orig. **86**, 472.

[**Klarenbeek, A.** (2). Recherches expérimentales avec un spirochète se trouvant spontanément chez le lapin et ressemblant au *Treponema pallidum*. [**Experimental researches with a spirochaete occurring spontaneously in the rabbit and resembling *Treponema pallidum*.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 326.

These two papers are identical in matter and refer to five rabbits which showed some inflammatory changes which had occurred spontaneously in the perineum and genital organs. In the lesions spirochaetes were found closely resembling *Treponema pallidum*. Tissue containing spirochaetes was found to be infective when introduced into a scarification in the perineum, skin of the back, eyelid, the eyeball, or testicle. Intravenous inoculation was unsuccessful. In one case a general infection occurred about 10 weeks after an intra-ocular and intratesticular injection of spirochaetes. One spontaneous infection was also observed in a cage. The disease in question is the same as that described in 1914 by Arzt and Kerl, by Jacobsthal in 1920, and by Levaditi and Marie in 1921 (vide *Medical Science*, 1921, **4**, 569). W. B.

Ronca, V. Ricerche istologiche in rane sottoposte all' ablazione del fegato. [**Histological investigations on frogs deprived of their liver.**] *Arch. per le sc. med.*, 1921, **44**, 45.

Frogs may survive even for a fortnight after the surgical removal of the liver. The organs most affected by the operations are the kidneys, in which a diffuse congestion and intense degenerative changes of the epithelium of the uriniferous tubules are seen. Important alterations are also found in the central nervous system; these consist of a diffuse chromatolysis associated with vacuolization of the cytoplasm, atrophy, and pyknosis of the nucleus. In the blood, the haemoglobin content is diminished, while the metachromatic substance of the 'granulo-filamentous erythrocytes' is increased. In the pancreas, limited parenchymatous changes are sometimes observed, but the secretory function of the organ does not appear to be affected. In the congested spleen, a fragmentation of the red corpuscles of changing intensity can be noticed. In the intestine a marked congestion is found, but no histological alteration of the epithelium and muciparous glands. C. d. F.

Sormani, C. (1). Ricerche sperimentali sull' ittero locale. [**Experimental investigations on local jaundice.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 55.

Sormani, C. (2). Sulla patogenesi dell' ittero emolitico. [**On the pathogenesis of haemolytic jaundice.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 63.

Sormani, C. (3). Ricerche sperimentali sull' ittero ematogeno. [**Experimental investigations on haematogenous jaundice.**] *Boll. d. Soc. med.-chir. di Pavia*, 1919, **32**, 575.

A haemolytic jaundice can be caused in dogs by subcutaneous or intraperitoneal injections of blood. This is due to a transformation of the haemoglobin into bilirubin and manifests itself under the form of pleochroism followed by urobilinuria and choluria. The absence of biliary pigments in the place where injections were made is against the hypothesis of a local biligenesis. If by the same experimental conditions the hepatic circulation is suppressed by ligature of the hepatic artery, biliary pigments are no longer found in the urine : hence the conclusion that the liver is necessary for the transformation of the injected blood into pigments.

To study more intimately the pathogenesis of haemolytic jaundice, the author had recourse to injections into dogs of dog's laked and isotonized haemoglobin, thus avoiding the haemolytic effect of distilled water and of the poisons generally used for this kind of experiment. The animals were killed at various periods of time from the beginning of the experiment, but in every case after bilirubin had begun to appear in the urine. The histological examination of the liver of the animals experimented upon showed that by the author's method both the liver and Kupffer cells remain unaltered, while the bile-ducts are greatly distended by bile quantitatively increased because of the injected haemoglobin and its transformation into biliary pigments. From these facts the author draws the general conclusion that by haemolytic just as by hepatogenous jaundice the essential cause for the passage of bile into the general circulation is stasis, the difference consisting merely in the degree. C. d. F.

Condorelli, L. 'Trichoblastomycosis axillaris.' [**Axillary trichoblastomycosis.**] *Ann. d'ig.*, 1920, **30**, 691.

The author has been able to find in the literature only one case (Waldeyer, *Atlas der Haare*, 1884), similar to that which he has observed in his own person. The disease is due to a blastomyces, which Condorelli was able to isolate from the hairs of the axilla, and for which he consequently proposes the name *Trichoblastomyces axillaris*, the term *trichoblastomycosis* being applicable to the disease. This is characterized by the presence, all along the hairs, of small nodules which have the colour and consistence of beeswax, and are easily detached from the hairs. These characteristics are sufficient to distinguish the disease clinically from all other nodular affections of the hairs with the exception of trichomycosis nodosa tropica (Castellani) and particularly its variety *alba*. For the discrimination between trichoblastomycosis and trichomycosis one must have resort to microscopic examination, though trichomycosis has never been observed in Europe.

Trichomyces axillaris is easily isolated by means of cultures in 3 per cent. agar with 5 per cent. of malt-extract. It quickly produces gaseous fermentation of glucose, levulose, maltose, and slowly also of lactose. It grows vigorously at 37° C. in most media when slightly acid, best on acid potatoes. It is very resistant to desiccation, but it is killed by heating for one minute at 60° C. It stains with almost all common aniline dyes, and is Gram-resistant. Condorelli was able to obtain the development of *Trichomyces* and the formation of the characteristic nodules on human hairs *in vitro.* C. d. F.

Puntoni, V. La pluralità del virus rabico. [**Plurality of rabies virus.**] *Ann. d'ig.*, 1921, **31**, 27.

It is generally held that there is only one virus of rabies, and that the inoculation of the same street virus into various animals of the same species may cause both the furious and paralytic forms of the disease. In fact the fixed virus vaccinates against that of the street. However, the author by chance came across a virus of the street termed by him No. 223, which showed a peculiar individuality of its own, when compared with other virus of the street and with that commonly used in the Antirabic Institute of Rome. It is interesting to note that the infection caused by virus 223, when inoculated subdurally into rabbits, could be prevented only by an autovaccine, but neither by the usual vaccine prepared with fixed virus nor by other vaccines prepared with virus of the street. C. d. F.

Puntoni, V. La tossicità dei vaccini antirabici. [**On the toxicity of antirabic vaccines.**] *Ann. d'ig.*, 1921, **31**, 201.

In the summer of 1919, during a series of antirabic inoculations into rabbits, the author observed no less than ten times that death supervened immediately after a subcutaneous injection of the usual dose (2 c.cm.) of carbolized virus. This sudden death appeared due to a massive coagulation of the blood in the right ventricle of the heart in consequence of the accidental and direct penetration of a rather large quantity of virus into the circulatory system. As a matter of fact the phenomenon could be, up to a point, prevented, if great care was taken not to hit veins when making subcutaneous injections of the virus; and it could be re-obtained whenever desired by injecting the virus into the marginal vein of the rabbit's ear. A few months afterwards Remlinger (*Compt. rend Soc. de biol.*, 1919, **82**, 1098) noticed a similar occurrence in rabbits inoculated subcutaneously with rather large doses of homologous nervous substance whether rabid or not. This, however, did not happen when cerebral substance of guinea-pigs was subcutaneously injected into rabbits or cerebral substance of rabbits or guinea-pigs into guinea-pigs. In a subsequent paper Remlinger (*Ann. de l'Inst. Pasteur*, 1920, **34**, 650) described and discussed at length the same facts, without being able, however, to express any definite opinion on their causation. On the other hand, Puntoni was aware that Cornwall (*Indian J. M. Research*, 1919, **6**, 237) had shown that the intravenous inoculation of carbolized virus from rabid rabbits into sheep was followed only by a temporary fall of the blood-pressure. All this led Puntoni to make a series of homologous and heterologous inoculations of rabid and non-rabid cerebral substance into various animals.

The results obtained may be summarized as follows: intravenous injections of antirabic vaccines are toxic in the same measure as emulsions or extracts of nerve organs of the same concentration. The presence of the virus of rabies does not increase the toxicity of an emulsion of nervous substance. The various antirabic vaccines commonly used vary in toxicity for the rabbit. The most toxic are those prepared with fresh nervous substance (fresh *virus fixe*, carbolized virus, sero-vaccine); the least toxic are those consisting of material either desiccated or warmed, or treated with ether. The inoculation of emulsions of nervous substance from different animals into others of the same or different species shows that there are two degrees of toxicity. These can be distinguished as the greater and lesser toxicity. The greater toxicity is always fatal, and manifests itself in the rabbit and dog after homologous inoculations of nerve emulsions. It is characterized clinically by symptoms identical with those of acute asphyxia; pathologically by a coagulation of the blood within the organs of the pulmonary circulation. The lesser toxicity is generally transient in character and may be observed in the guinea-pig and rat after injections of homologous nerve-emulsions. It manifests itself in the form of motor troubles such as clonic contractions, tics, transitory paresis of the four limbs. The animals, in which the phenomena of greater toxicity can be observed, are affected in the same way by cross-inoculations; but those which do not show such a picture after homologous inoculations are not differently affected by inoculations of heterologous material. From a general point of view it can be held that a nerve-emulsion which fails to cause manifestations of greater toxicity in the homologous species, does not cause them in any other one. Phenomena of greater toxicity in one sense only never were observed. Men may be safely treated with rabbit's virus, probably because emulsions of human nervous substance fail to cause the phenomena of greater toxicity when inoculated into rabbits. These only show the transitory symptoms of lesser toxicity just as men are occasionally subject to various disturbances during and after an antirabic treatment. The greater toxicity cannot be explained as due to a sort of anaphylatoxin, viz. to the contact, *in vivo*, of the blood-plasma with the minute particles out of which a nerve-emulsion results. On the contrary, a generous addition of rabbit's serum to a homologous nerve-emulsion prevents this from being toxic for the same animal. This also happens if the emulsion is heated, but not if its reaction is experimentally altered. The greater toxicity is easily caused by intravenous injections of even minimal doses; larger ones are necessary to provoke it by means of intra-arterial injections, and still larger ones if the inoculations are intraportal. The lesser toxicity is independent of these various factors. The cause of these striking differences in the action of various emulsions or extracts of nervous substance remains at present entirely unknown.

C. d. F.

Bertarelli, E. Tentativo di trasmissione della malaria al macaco. [**Attempt at transmission of malaria to *Macacus*.**] *Ann. d'ig.*, 1920, **30**, 689.

Experiments were made with citrated blood of patients affected by tertian and aestivo-autumnal malarial fever. This was, at different periods, injected intravenously and intraperitoneally into a *Macacus cynomologus*; but all attempts to induce infection were attended by negative results.

C. d. F.

Volpino, G. Ricerche preliminari sulla coltivazione del 'virus vaccinico'. [**Preliminary investigations on the cultivation of vaccine virus.**] *Gior. d. r. Acc. d. med. di Torino*, 1921, **84**, 20.

Glycerinated vaccine pulp was used as material. The culture medium was prepared from human, unheated blood-serum, diluted with an equal volume of water and added in the proportion of 2 c.cm. to each of a series of test-tubes containing agar solidified in a slanting position and in such a way that when the tubes were kept straight part of the agar had no contact with the added serum. These tubes were inoculated by means of a loopful of vaccine pulp introduced into the serum, while either a fragment of the same pulp or a saprophytic germ was smeared on the free portion of the agar. The tubes were plugged with cotton-wool and paraffin, or otherwise put in a semi-anaerobic condition, and then kept for 15 to 30 days in an incubator at 37° C. Subcultures were obtained by taking a drop of the fluid from each tube of the first series and sowing it in each of a second series of tubes prepared and treated in the same way as before. After another 15 or 20 or 30 days a third passage was made, and so on up to the 11th. During this series of successive subcultures the vaccine did not lose its virulence. This was tested by means of corneal vaccinations into rabbits, in which a typical keratitis developed after four or five days. The vaccine obtained from the corneal lesions was transmissible in series to other rabbits, and in the affected portions of the successfully inoculated corneas Guarnieri's bodies and 'intracellular mobile corpuscles' were seen in large numbers.

The author draws from these results the conclusion that it is possible to cultivate the vaccine virus in symbiosis with saprophytic germs. Pure cultures, in the usual sense of this term, were not obtained. But a vaccine, still virulent, was obtained by passing through a Berkefeld filter the fluid portion of mixed cultures, and then inoculating the filtered fluid into tubes prepared as above, but not smeared with any saprophytic germ. The cultures thus obtained still caused a typical keratitis in the rabbits' cornea in which Guarnieri's bodies and 'intracellular mobile corpuscles' were found over again. This confirms the view that vaccine belongs to the group of filter-passing viruses and proves that after filtration it still maintains the power of multiplying, *in vitro*, in conditions similar to those of pure cultures.

The microscopic examination of the fluid portion of all these cultures and subcultures revealed the presence of minute granules stainable by Löffler's method for bacterial flagella, and similar to those described by Paschen, and by him considered as specific of variola and vaccinia. Volpino, however, thinks that these granules are not specific and, very likely, are not even micro-organisms. He adds that, in spite of the opinion of Paschen, Lipschütz, and other authors, such granules probably have nothing in common with the 'intracellular mobile corpuscles' observed by him within the cells of the vaccinated rabbits' cornea by means of both the dark field illumination and Giemsa's methods, the last one of which stains them blue. These corpuscles are, according to Volpino, something certainly specific; while the granules shown by Löffler's flagella stain, as well as those of Paschen, may be confused with colloidal precipitations or protein granules frequently found in organic fluids. C. d. F.

Azzi, A. Azione degli stimoli termici cutanei sulla temperatura dell'aria espirata. [**Action of cutaneous thermal stimuli on the temperature of the expired air.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 49.

The present research forms part of a series of investigations to which reference has already been made (see Viale, G., *Medical Science*, 1921, **3**, 371, and Azzi, A., *ibid.*, 1921, **4**, 167). Azzi has now made a new set of experiments with the following results: there is a strict relation between the temperature of the expired air and the subjective sensation of cold consequent upon the application of a cold stimulus on a circumscribed area of the skin. The phenomenon can be noticed a few instants after the application of the stimulus, and the sooner the lower is the temperature of the stimulus in comparison to that of the stimulated area. The temperature of the expired air reaches a minimum in a few minutes, to become somewhat higher after a little while, but it very seldom reaches its original level. This happens, however, whenever the initial diminution is very small; but in such cases the sensation of cold also disappears. The intensity of the phenomenon changes according to the sensitiveness of the subject and the situation of the stimulated area. Most effective are the stimulations of the skin of the face and foot, of the flexor surface of the hand, forearm, and limbs in general. Similar facts can be observed also after the application of warm stimuli to circumscribed areas of the skin, though the subsequent variations in the temperature of the expired air are not so constant and regular as in the case of cold stimuli.

These results are not without importance for the pathogenesis of affections of the respiratory organs subsequent to the sudden refrigeration of even limited portions of the body surface. In this respect one may recall the recent investigations of Mudd, Grant, and Goldman (*J. Med. Research*, 1919, **40**, 53, and *J. Exper. M.*, 1920, **32**, 87), who have also found that chilling of the body surface causes vasoconstriction and ischaemia in the skin of the head and neck and in the mucous membranes of the palate, pharynx, and palatine tonsils. C. d. F.

Orr, P. F. Studies on *Bacillus botulinus*. I. Destruction of botulinus toxin by heat. *J. Med. Research*, 1921, **42**, 127.

This is a study of the action of heat on the filtered toxins of ten strains of *B. botulinus*. The author finds that all of them were comparatively thermolabile. At 80° C. they are destroyed in 30 seconds to 5 minutes; at 72° C. in 2 to 18 minutes, and at 65° C. in 10 to 85 minutes. The heating of any food material to the boiling-point will destroy all traces of toxin which may be present. W. B.

Lebailly, C. (1). Conservation du virus aphtheux par le froid. [**Preservation of the virus of foot and mouth disease in the cold.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1261.

Lebailly, C. (2). La fièvre aphtheuse bovine n'est pas transmissible à l'homme; la stomatite aphtheuse humaine n'est pas transmissible aux bovines. [**Bovine aphthous fever is not transmissible to man; human aphthous stomatitis is not transmissible to bovines.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1140.

Lebailly has attempted to test the truth of the statement found in most text-books that the foot and mouth disease of cattle can be communicated to man through contaminated milk. This statement is apparently based on some experiments carried out in Germany as far back as 1834.

During the epizootic of 1919 in Normandy he failed to discover a single case of human infection on farms, &c. On the other hand, between June 1920 and April 1921 he saw 10 cases of aphthous stomatitis in Caen. An inquiry into these cases and the sources of their milk supply failed to lead to any clear conclusions.

Lebailly next carried out the following experiments: the saliva, blood and contents of the bullae from each of three different cases of human aphthous stomatitis at different stages of the disease failed to transmit the disease to a calf, a heifer, and a young ox respectively, but some weeks later these same animals contracted foot and mouth disease on receiving an injection of the virus of that disease. On the other hand, a monkey (*Macacus cynomolgus*) failed to develop the disease on receiving an injection of virulent material from an infected ox. An assistant accidentally inoculated himself deeply with similar virulent material and no untoward effect resulted. Three human subjects next received subcutaneously varying doses of virulent material from an infected ox, and in addition some of this material was rubbed into their gums and buccal mucous membrane after previous scarification. At the same time for purposes of control a heifer received a subcutaneous injection of the same material. The heifer contracted the disease and died of it, whilst the human subjects remained perfectly well.

Lebailly concludes from the above that the aphthous fever of cattle and the aphthous stomatitis of man are two distinct entities, and that man is immune to the former and cattle to the latter. J. R. P.

SELLARDS, A. W., and BIGELOW, G. H. Investigation of the virus of measles. *J. Med. Research*, 1921, **42**, 241.

The authors found a small pleomorphic Gram-positive bacillus in the blood of 25 out of 31 cases of measles, especially when means were taken to prevent phagocytosis in cultures. In one case a positive result in culture was obtained from 0·01 c.cm. of blood. In a series of 24 control individuals morphologically similar bacilli were found in 5. Fermentation tests, however, showed that in at least three the bacteria were not identical, for the majority of the measles strains fermented glucose, dextrin, and in some instances saccharose, while three of the control stains failed to ferment glucose. Three monkeys (*M. rhesus*) were inoculated with strains from the measles cases. In two the symptoms were vague, consisting only of a diffuse erythema and isolated papules. In one case a distinct maculopapular eruption appeared over the abdomen followed next day by some dark red petechial spots. A week later this same animal was reinoculated, but developed no erythema or rash, whereas a control animal showed well-marked erythema of the face and chest after six days. Guinea-pigs and rabbits were insusceptible.

W. B.

TOZER, FRANCES. The effect on the guinea-pig of deprivation of vitamin A and of the antiscorbutic factor with special reference to the condition of the costochondral junctions of the ribs. *J. Path. & Bacteriol.*, 1921, **24**, 306.

The experiments described in this paper were undertaken to discriminate the effects on the guinea-pig of deprivation of the fat soluble A growth factor (vitamin A) from those caused by lack of antiscorbutic factor alone. The animals were fed on a basal diet of oats and bran, the antiscorbutic being orange juice while vitamin A was supplied in the form of milk autoclaved at 120° C. for 1 hour. Some animals were kept as controls, others were deprived of antiscorbutic, or vitamin A while others had neither antiscorbutic nor vitamin A. After varying intervals from 10 up to 100 days the animals were killed, special attention being directed to the amount of fat, the presence of haemorrhages, the condition of the bones, teeth, and internal organs. The ribs of all animals were examined histologically, and their condition is described in the paper. When the antiscorbutic factor is withheld from the diet the animals after the first fourteen days begin to show symptoms which are more or less characteristic, and die about the thirtieth to the thirty-fifth day. When vitamin A alone is withheld the animals lose weight, the bones become fragile, and the teeth brittle but not loose. When both accessory food factors are withheld from guinea-pigs no symptoms are observed under fourteen days, except that the animals do not thrive. The joints become swollen and symptoms analogous to scurvy develop and cause a fatal issue. A table setting out the symptoms and bone changes in the three experimental diseases is presented in the paper, and an attempt is made to differentiate true scurvy symptoms from those caused by the withdrawal of vitamin A from the dietary. W. B.

BIOCHEMISTRY

Fischer, H. Über den Mechanismus der Goldsolreaktion in Liquor cerebrospinalis. [**The mechanism of the colloidal gold reaction in the cerebrospinal fluid.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **14**, 60.

This extensive paper concerns itself with a critical analysis of the colloidal gold reaction in relation to the diagnosis of syphilis. Since Lange's paper, which appeared in 1912, the attention of many immunologists has been directed to the interesting phenomenon which Lange claims to be diagnostic of syphilitic infection, and one author (Spät) looks upon it as a model of an immunity-reaction. As is well known, the reaction is one in which the syphilitic immune body in the cerebrospinal fluid is asserted to produce with colloidal gold solution an agglutination. The reaction is said to be particularly efficient in syphilitic infection of the central nervous system.

In the first place the author points out that if the action is due to certain ferment-like substances all enzymes are colloidal, and hence all difficultly diffusible; that enzymes have not, as yet, been prepared in a pure state, and that in being precipitated they carry with them foreign substances. Hence the chances that one may definitely ascribe a particular reaction like the present one to a specific ferment such as fibrin ferment are practically zero.

In the experimental work a colloidal gold preparation was made by treating a gold solution with acrolein. It is possible in this way to prepare bright red gold dispersions without the difficulties attendant on the reduction by glucose or formalin, or by the electric arc. The principle of the method was to treat the gold solution with varying concentrations of the fluid to be tested. The colour was plotted against the dilution. Satisfactory graphs were obtained in this way. The colloidal gold experiments were controlled by Wassermann tests.

In a comparison of fresh cerebrospinal fluid, of C.S.F. from cases of progressive paralysis and of epidemic meningitis, normal serum and serum from a secondary lues, and of the supposed luetic reduction body extracted from the liver treated with syphilitic serum and C.S.F. and the extracts of normal serum and luetic serum, it emerges that physiological saline which gives no Wassermann reaction gives a gold curve similar to that of G.P.I. Hence the syphilitic reacting compound is not the same as that giving the colloidal gold precipitation in paralysis. One also obtains a decided gold reaction in C.S.F. of cerebrospinal syphilis giving a negative Wassermann reaction.

In order to ascertain what fraction of the C.S.F. is responsible for the gold reaction, 30 c.cm. of the fluid was fractionally precipitated with ammonium sulphate by neutral and by acid reaction, the precipitates dialysed and used for the test. The concentration in protein was controlled by micro Kjeldahl analyses and by the refractometer. The results were as follows: the four globulin fractions precipitated colloidal gold. The alkali soluble parts of the globulin fractions gave maximal lower concentration. This is the point which Lange asserts differentiates non-syphilitic affections of the central nervous system from those which are specific. The euglobulin and pseudo-globulin fractions have the most intense action on colloidal gold. The curves of the globulin fraction show an unmistakable similarity with the results obtained from syphilitic C.S.F.

The albumin fractions showed no tendency to precipitation, in fact they inhibit the precipitation by the globulins; they also protect the gold from precipitation by electrolytes such as sodium chloride.

The fibrinogen and fibrinoglobulin fraction gave a smaller precipitation intensity than pseudo-globulins. While the amount of inorganic electrolytes in the fluid is insufficient to produce a precipitation, they intensify the action of the globulins present. The amount of precipitation produced by a cerebrospinal fluid is practically proportional to the amount of globulins present. The optimum is due to the quantitative relations of the electric charges on the gold and on the globulins respectively. The view of Spät, that the colloidal gold reaction is dependent on the syphilitic component of the fluid, is not confirmed. Only in certain cases does the gold reaction run parallel with the Wassermann reaction, and hence the formation or secretion of the immune body does not under all circumstances keep pace with the exudation of globulins in the cerebrospinal fluid. C. G. L. W.

Bonsmann, M. R. Über die Verwendung der in Körperflüssigkeiten vorhandenen Schutzkolloide beim Kongorubin. [**Protective colloids in body fluids and congo rubin.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 66.

Congo rubin is a substance allied to congo red, and experiments show that it can be used for reactions of the colloidal gold type. With it one can differentiate fluids of the type of hydraemic transudates, stasis transudates, and exudates. It shows that protective colloids other than albumin are present in the cerebrospinal fluid. C. G. L. W.

Hoffmann, H. Der Einfluss vom Hinterlappenextract der Hypophyse auf die Wasserabscheidung der Magenwand. [**The influence of extract of the posterior lobe of the pituitary on the secretion of water in the stomach.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **12**, 134. (*Physiol. Abstr.*, 1921, **6**, 212.)

The injection of pituitary extract into healthy subjects caused an increased secretion of water into the stomach. This water contained no enzyme, protein, or mucus, and little or no HCl. It is stated that the effect is not due to the activity of the gastric glands, but to a secretory action of the capillary endothelium. J. H. B.

Ellinger, P. Über den Einfluss der Nervendurchschneidung auf die Wasser- und Salzausscheidung durch die Niere. [**On the influence of nerve section on the excretion of water and salts by the kidney.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 77.

The nervous influences which reach the kidney follow the paths of (1) the vagus nerves; (2) the greater splanchnic nerves; (3) the abdominal sympathetic. The general nature of the impulses following these three paths is the same—that is to say, it is inhibitory. When they are divided excretion is increased. J. H. B.

Austin, J. H., Stillman, E., and **Van Slyke, D. D. Factors governing the excretion rate of urea.** *J. Biol. Chem.*, 1921, **46**, 91.

The work forms a significant extension to the work of Ambard and his collaborators. It was shown by them that the rate of urea excretion is a function of both the concentration of urea in the blood as well as the concentration of urea in the urine. It is only when these have been taken into account, therefore, that the rate of excretion of urea can be taken even as an approximate indication of the functional capacity of the kidney.

The work in this paper establishes the fact that it is of more importance to take the rate of volume output in the urine as one of the factors than the concentration of urea in the urine. Expressing the result in the words of the authors: 'The rate of urea excretion per unit of body-weight in a normal dog or man increases approximately (*a*) in simple direct proportion to the blood urea concentration, and (*b*) in proportion to the square root of the rate of volume output of urine per unit of body-weight, as long as the volume rate remains within ordinary limits.' This increase in rate does not hold, however, after a certain limit of volume output, which is between 3 and 6 litres per 24 hours for the normal individual studied. Increase over this limit does not further accelerate urea excretion.

The relationships obtained by the authors are expressed in the following equation:

$$K = \frac{D}{B\sqrt{\frac{V}{W}}} = 7{\cdot}5 \pm 3 \text{ (for normal man).}$$

Here D = urea output (in gm. per 24 hours).
B = blood urea (gm. per litre).
V = volume output (litres per 24 hours).
W = body-weight in kilos.
K = excretory constant.

For values of V above the augmentation limit, the value of the augmentation limit A replaces V in the formula. R. A. P.

HILDEBRANDT, F. Über den Einfluss der Vagusdurchschneidung auf die Zuckerausscheidung in der Niere. [**On the influence of vagotomy on sugar excretion by the kidney.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 142.

The author produced hyperglycaemia in rabbits by injecting adrenalin, and observed how great the hyperglycaemia had to be before sugar appeared in the urine. He then cut both vagi in these rabbits, and, after they had recovered from the operation, carried out the experiments again. He observed that after operation sugar appeared in the urine when the percentage of sugar in the blood was very much less than before. He concludes that the vagi assist in keeping high the leak-point of the kidney for sugar. J. H. B.

SCHMIEDEBERG, O. Über die Vorgänge bei der Zuckerausscheidung im Diabetes. [**On the processes concerned in the excretion of sugar in diabetes.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 1.

This paper contains an interesting account of Schmiedeberg's views on the nature of diabetes. He begins by quoting evidence to show that the excretion of sugar by the kidney is quite independent of the percentage of sugar in the blood. Very large amounts indeed can be injected without any proportionally significant glycosuria following. When large amounts are injected there is a change in the composition of the blood, and this change may reasonably be expected to alter kidney function. Such glycosuria as then occurs is due to the altered kidney function, and not to the hyperglycaemia itself.

Next he recounts observations which suggest that in diabetic conditions dextrose is built up into an incombustible complex with some product of protein breakdown. The work of Straub and Rosenstein showed that CO poisoning produced glycosuria in fasting dogs in certain conditions. Feeding dextrose led to no excretion of sugar, but feeding with a pancreatic digest of fibrin at once produced glycosuria. Similarly the experience of Naunyn and of Falta and Gigon leads them to attach much more importance to the diminution of meat and protein generally in the diet of diabetics than to the exclusion of carbohydrates.

Diabetes, then, is due to the formation of a compound of dextrose with a product of protein metabolism. The kidney can split this compound and liberate the sugar in the urine. The compound is not observed in the blood because the processes of blood-sugar estimation set free the dextrose from the combination. It is the normal function of the pancreas to inhibit the formation of such an incombustible substance. In diabetes the liver can still form glycogen from levulose (Minkowski), and the usual absence of glycogen formation is not due to loss of liver function. Schmiedeberg considers that adrenalin diabetes occurs as a result of a paralysis of pancreatic function, but that phloridzin acts simply on the kidney, so that after phloridzin, sugar is excreted from the blood just as is urea. J. H. B.

STEPP, W. Kritisch-analytische Betrachtungen und Untersuchungen zur Bestimmung des wahren Blutzuckers bei Gesunden und Kranken. [**A criticism and investigation of the methods of estimating the true value of the blood-sugar in healthy and diseased subjects.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 105.

The author has investigated the blood-sugar percentage in 123 subjects by the different methods available. He concludes that polarimetric determinations, or values obtained by fermentation methods, are accurate, for these agree with one another. Technique depending on the reducing power of blood for the estimation of dextrose gives results which are 20–40 per cent. too high, and in some cases the error is as great as 100 per cent. J. H. B.

Cooper, E. A., and **Walker, H. The nature of the reducing substance in human blood.** *Bio-Chem. J.*, 1921, **15**, 415.

The problem of sugar excretion in diabetes is complicated by the fact that we are not sure as to the carbohydrates circulating in the blood, both as to their character and their possible combinations with other substances. The authors have subjected the MacLean estimation to critical examination. They find that the reducing substances in the blood are destroyed by boiling with ammonia as are reducing sugars. The reducing power of the blood is increased by acid hydrolysis, indicating the presence of complex substances yielding reducing substances on splitting. The actual amount of increase is difficult to determine owing to destructive and retarding action of the process of hydrolysis and subsequent neutralization. C. G. L. W.

Gram, H. C. *Studier over Fibrinmængden i menneskets Blod og plasma samt nogle hermed forbundne problemer.* [***Studies on the fibrin content in human blood and plasma and some allied problems.***] Copenhagen, Steen Hasselbalch's Forlag, 1921, pp. 276.

This thesis contains an English summary from which the following notes are taken. A bibliography of 169 references to blood-clotting is appended.

The blood used was citrated and the clotting determined after the addition of the necessary amount of calcium chloride. A method is described by which the fibrin content of plasma or blood can be determined in 2 c.cm.

The fibrin content of plasma in normal men varies between 0·2 and 0·36 per cent., in women 0·21 and 0·38 per cent. The fibrin content of blood varies between 0·11 and 0·19. In a large number of diseases the fibrin content was within normal limits. A diminution is found in a few cases of pernicious anaemia. Where there were parenchymatous changes in the liver the fibrin content was low. The findings seem to support the theory of the origin of fibrinogen in the liver. No evidence has been found to indicate that the haemorrhagic diathesis is caused by a fibrin deficiency.

An increased fibrin percentage is found in certain infectious diseases (pneumonias, suppuration), while in typhoid, influenza, tuberculosis, and syphilis it is missing. It is also high in uncompensated diseases of the heart, nephritis, and malignant tumours. In pregnancy there is an increased concentration of fibrin. The author seeks to relate the high content with irritation of the liver. He looks upon a decreased fibrin content as of bad prognostic significance. C. G. L. W.

Fuhrmann, L., und **Kisch, B.** Vergleichende Untersuchungen bei Mutter und Neugeborenen. Beobachtungen über Oberflächenspannung des Serums und Hämolyse. [**Comparative tests of maternal and infant blood and serum. Surface tension and haemolysis.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 84.

The blood of new-born children clots more slowly than that of the mother. The colour of the serum is more orange, which also applies to foetal serum. The surface tension is lower. The surface tension of eclamptic serum is low and is the same as that of the new-born. In cases which return to normal after delivery there is an increase in surface tension. The authors were not able to make out any difference between maternal and infant bloods in their resistance to haemolysis produced by alkali salts.

C. G. L. W.

Jodlbauer, A., und **Haffner, F.** Über die Wirkung von Eosin und Rose bengale auf rote Blutkörperchen und den Zusammenhang von Aufnahme und biologischer Wirkung. [**The action of eosin and rose bengal on red blood corpuscles, and the relation between uptake and biological effect.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 243.

The toxicity of fluorescein derivatives in the absence of light is increased when iodine is substituted for bromine or chlorine: thus rose bengal (tetrachlor-tetraiodofluorescein, Na salt) is 100 times more powerful as a haemolytic agent than eosin (Na salt of tetrabromfluorescein). An attempt was made to find out how far this difference was due to the different extent to which the two dyes were taken up by the cells, and it was found that the different effects were due entirely to the greater ease with which the rose bengal was adsorbed. The reaction of the solution was also of importance—the more acid the solution the more readily was the dye adsorbed, and the more readily haemolysis was produced. The effect on the corpuscles was a typical alteration of the colloids by the effect of the anion, haemolysis being caused by increased hydration. The uptake of the dyes followed the law of adsorption. C. L. E.

Abderhalden, E., und **Kürten, H.** Untersuchungen über die Aufnahme von Eiweissabkömmlingen (Peptone, Polypeptide, und Aminosäuren) durch rote Blutkörperchen unter bestimmten Bedingungen.) [**The uptake of protein derivatives (peptone, polypeptides, and amino-acids) by red corpuscles under certain conditions.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 311.

Washed ox corpuscles were suspended in a slightly hypertonic solution of NaCl containing the protein derivative under investigation for 45 minutes at room temperature. After centrifugation, the amino-nitrogen of the clear fluid was estimated by Sörensen's method, the reduction of amino-N giving the amount of amino-acid taken up. Glycine, alanine, *d-l*-valine, *d-l*-leucine, *l*-tryptophane, glycyl-*d*-isovaline, *d-l*-leucyl-glycine, *d-l*-leucyl-glycyl-glycine, and silk peptone were used in the various experiments, and all were taken up in accordance with the laws of adsorption. Apparent exceptions provided by leucine, the polypeptides, and peptone were due to the fact that these caused agglutination of corpuscles, so that the uptake was smaller for the higher concentrations: but if the suspension was shaken to reduce the agglutination, normal or almost normal values were also obtained for these substances. It is pointed out by the authors that the adsorption does not necessarily hold under conditions other than those of their experiments, or for other blood corpuscles. Thus horse corpuscles gave irregular results. C. L. E.

Lamson, P. D., and **Roca, J.** **The liver as a blood-concentrating organ.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 481.

In previous articles the authors have shown that in acute polycythaemia the sudden increase in red cells takes place in the liver, and that the process is one of blood concentration due to the escape of fluid into the liver lymphatics. Measured amounts of saline were injected at definite rates into dogs under ether anaesthesia. The experiments were done on normal animals, those with an Eck fistula and the hepatic artery tied, thus cutting off the blood-supply to this organ. Adrenalin was used in both these preparations. The blood concentration was measured as haemoglobin.

The disappearance of isotonic salt solution when injected is partly due to the liver. The rate of disappearance is more than four times decreased by removal of the organ. The rate of disappearance is increased when adrenalin is added to the salt solution. This action is due to the presence of a vasoconstrictor mechanism on the venous side of the organ. Obstruction to the hepatic flow causes increased filtration throughout the liver capillary area. After a latent period this fluid returns to the general circulation by way of the thoracic duct. The addition of adrenalin to intravenous salt infusion for the purpose of raising the blood-pressure should be discouraged, as it accelerates fluid loss. C. G. L. W.

Rogoff, J. M., and **Goldblatt, H. Attempt to detect thyroid secretion in blood obtained from the glands of individuals with exophthalmic goiter and other conditions involving the thyroid.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 473.

Tadpoles were used as the test object. A specimen of thyroid blood was collected at the time of operation, and systemic blood obtained some time later. The specimens were dried at 50° C. to 55° C. With the dried specimens tadpoles were fed and the growth noted. No evidence of any active thyroid material was obtained in any of the bloods. C. G. L. W.

Frisch, A., und **Starlinger, W.** Chemisch-physikalische Blutuntersuchungen zur Frage der Protoplasmaaktivierung. [**Physico-chemical investigations on protoplasm activation.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 142.

Weichardt asserts that the introduction parenterally of foreign protein into the body leads to increased vitality. This increase is due to the raising of the activity of the organs. The same statement is made of the action of Röntgen rays and diathermy.

The authors have taken the formation of fibrinogen as an indicator of increased organic activity. The foreign proteins used were tuberculin, milk, and horse-serum. Certain control experiments were made with X-rays. The immediate sequence of all these operations is an increase in fibrinogen, with a later fall in the amount. There was also a decrease in the coagulation time of the blood. The effect took place in the first hours after treatment. They regard the process as one of tissue breakdown which leads to the formation of fibrinogen. The effect is not one in which the body-cells are excited to increased activity. C. G. L. W.

Telfer, S. V. The influence of free fatty acids in the intestinal contents on the excretion of calcium and phosphorus. *Bio-Chem. J.*, 1921, **15**, 347.

There has been some conflicting evidence regarding the relation between the nature of the fat in the diet and the excretion of calcium. It seems that there is a possible close relationship between the nature of the fat and calcium retention. If this be so, there is obviously an important connexion between the nature of the fat used for feeding infants and the pathogenesis of rickets.

Normal cases and those suffering from biliary atresia and jaundice with syphilitic hepatitis, were studied to ascertain the relation between fat excretion and the distribution of calcium and phosphorus in the faeces and urine. The subjects were infants. In complete exclusion of bile from the gut over 70 per cent. of the dried faeces may consist of fatty derivatives.

The persistence of an excess of fatty acids in the intestine is associated with an excess of calcium soaps in the intestine. The phosphorus is eliminated as phosphates in the urine. The degree to which the normal excretion of calcium and phosphorus can be varied depends on the concentration of free fatty acids in the intestine. C. G. L. W.

Fellner, O. O. Über die Wirkung des Placentar- und Hodenlipoids auf die männlichen und weiblichen Sexualorgane. [**The effects of placenta and testis lipoids on the male and female sexual organs.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 199.

Lipoids prepared from placenta, ovary, or corpus luteum, when injected subcutaneously or intraperitoneally produce enlargement of the mammary glands, uterus, &c., in the female; in the male a degeneration of the testis and epididymis results, so that these return to the immature condition present at birth. Injection of testicular lipoid produces similar effects on the female to those seen with placenta or ovary extracts, while on the male the effect is to produce degeneration of the generative portions of the testis, with increase of interstitial cells. There follow some speculations regarding the functions of the 'female sexual lipoid' in the testis. C. L. E.

Backmann, E. L. Die Erregung des überlebenden Uterus und Darmes durch Organextrakte und -dialysate, &c. [**The stimulation of the surviving uterus and intestine by organ extracts and dialysates, &c.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 261.

Extracts of uterus, intestine, and muscle, in water, saline solution, or alcohol, cause contraction of the isolated uterus and intestine. The active substance is apparently not choline. Aqueous extracts of blood, especially of fresh blood, have a similar action. (The author does not seem to have considered the possibility of the presence of histamine or related bodies.)
C. L. E.

Rother, J., und **Szegö, E.** Über die Beeinflussung der Harnsäure-ausscheidung durch Röntgenbestrahlung der Thymusdrüse. [**The effect of X-rays on the thymus in relation to uric acid elimination.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 262.

By treating the thyroid with X-rays there was no change in the elimination of uric acid. When the thymus was irradiated there was a notable increase in the amount of uric acid eliminated. These results were only obtained in cases where Basedow symptoms were evident. In normal cases no such effect was obtained. If the cases were those where the symptoms of exophthalmic goitre were not acute the variations in uric acid excretion were within normal limits. In an operated case where a large thymus was found a very large increase in uric acid was obtained as the result of treatment with X-rays. C. G. L. W.

Cameron, A. T., and **Carmichael, J. Contributions to the biochemistry of iodine. 4. The effect of thyroxin on growth in white rats and rabbits.** *J. Biol. Chem.*, 1921, **46**, 35.

It has been previously shown by the authors and others that the inclusion of thyroid in the diet of rats and rabbits leads to a decrease in the rate of growth, as well as to the hypertrophy of certain organs such as the heart, liver, kidneys, and adrenals. This effect cannot be produced by sodium iodide alone, or by feeding with thymus, pineal, or pituitary. The feeding of adrenal tissue by Hoskins led to a hypertrophy of the testis, and not the thyroid. As the effect of thyroid feeding was so specific, the authors have used the effects as a test for the identity of thyroxin, the tryptophane iodine compound isolated by Kendall from the thyroid gland.

The thyroxin was found to produce the effects of the desiccated thyroid tissue. It was observed also that there was a large increase of lymphatic tissue. It is to be noted, however, that the thyroxin when compared with the same iodine content of thyroid tissue was distinctly inferior. This was attributed by the authors to bacterial decomposition in the intestine. They consider that the hypertrophy of the heart and lymphatic tissue resembles that found in hyperthyroidism. R. A. P.

Hastings, A. B., and **Murray, H. A. Observations upon parathyroidectomised dogs.** *J. Biol. Chem.*, 1921, **46**, 233.

Three theories of the causation of the tetany following removal of the parathyroids are given. Firstly, that the symptoms are due to a disturbance of salt metabolism, especially calcium (Loeb and MacCallum). Secondly, that they are due to alkalosis (Wilson, Stearns, and Thurlow), and thirdly, that they are due to the accumulation of guanidin compounds in the blood as the result of a profound disturbance of the protein metabolism (Paton, Findlay, and Burns). For the latter view there has been good evidence accumulating lately. In the present research, the authors could not demonstrate a change in the alkaline reserve of the blood. They observed, however, quite constantly a fall in the Ca content of the blood. Tetany came on when the serum Ca reached a value of 7 mgm. per 100 c.cm. blood. Sugar analyses showed no significant changes in sugar metabolism. Several minor symptoms are recorded in some detail, which can be included under the heading of increased autonomic excitability. R. A. P.

Schade, H., **Neukirch, P.**, und **Halpert, A.** Uber lokale Acidosen des Gewebes und die Methodik ihrer intravitalen Messung; zugleich ein Beitrag zur Lehre der Entzündung. [**The local acidosis of tissues and their intravital measurement, and a contribution to the knowledge of inflammation.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 11.

The authors describe a very ingenious hydrogen electrode which one is able to introduce directly into superficial living tissues and allow to remain for some considerable time. The fluid drawn into the small apparatus can be equilibrated with mixtures of hydrogen and carbon dioxide. The technique of the operation is described in detail. They also describe an electrode on which measurements can be made of the hydrogen-ion concentration of very small pieces of tissue or quantities of fluid.

Measurements of subcutaneous normal tissue gave values (5·6 per cent. CO_2) P_H 7·09–7·24. With muscular effort there was an increase in hydrogen-ion concentration (rabbits). A large number of estimations were made of the acidity of the exudates of various inflammations. In acute infective abscesses highly acid values were found, as high as P_H 5·95 (furuncle). Chronic abscesses gave more alkaline reaction, while a pleural exudate from a carcinoma gave $P_H = 7{\cdot}09$. In ascites a practically normal value was obtained.

The buffer content of lymph is smaller than that of blood or serum, due to the decrease in the amount of albumins. The carbon dioxide partial pressure in the tissues is greater than in venous blood. Measurements made on cases of diabetic acidosis gave tissue-juice values which, with one exception, were normal. This the authors put down to the locality in which such measurements are taken. C. G. L. W.

Trendelenburg, W. Zur Methodik der Gewinnung von Alveolarluft. [**Methods of obtaining alveolar air.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 311.

Methods are described for obtaining alveolar air with the smallest possible dead space. Types of valves are very fully described. The results with the better class of valves are very close to those obtained by the Haldane-Priestley method. C. G. L. W.

Schall, L. Untersuchungen über die Methodik der Messung der Kohlensäurespannung in den Lungenalveolen. [**The measurement of carbon dioxide in the pulmonary alveoli.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 323.

A technical paper in which the influence of various types of valves, the influence of resistance, and valve pressure is discussed. The estimation of alveolar carbonic acid is dependent on the form and resistance of the valves employed. The method of additional breathing, in which a slight expiratory effort is made at regular intervals and samples of the air at the end of the effort are taken, gives somewhat higher carbon dioxide than with the valve method. The method has certain advantages over the Haldane-Priestley method of obtaining alveolar air. C. G. L. W.

Carpenter, T. M. Tables, factors, and formulas for computing respiratory exchange and biological transformations of energy. *Carnegie Instit., Washington*, 1921, **303**, pp. 123.

This book will be a very welcome time-saver to all engaged in metabolism work. The first ten tables are the usual ones for gas-correction. Tables 11 to 29 are those most likely to be of especial value. No. 11 gives the volumes of oxygen in incoming air corresponding to 100 volumes of outgoing air with different percentages of nitrogen, which will save a great deal of calculation. Table 13 gives calorific values of oxygen and carbon dioxide for non-protein respiratory quotients, and proportions of energy from carbohydrate and fat consumed. Table 14, the heat production per minute, hour, and day, calculated from oxygen consumption per minute at RQ=0·82. Tables 16 to 18 are for calculating body surface, while 19 to 29 are basal metabolism prediction tables. C. L. E.

Klinger, R. Beiträge zur pharmakologischen Wirkung des Guanidins. [**Contributions to the pharmacology of guanidine.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 129.

It is shown, in confirmation of other workers, that the symptoms of guanidine poisoning closely resemble the symptoms of tetany produced by para-thyroidectomy. While, however, tetany is relieved by the administration of calcium salts, the author is unable to detect any beneficial effect on the course of guanidine poisoning by calcium administration. J. H. B.

Frank, E., und **Alexander-Katz, R.** Zur Lehre vom Muskeltonus. I. Über die Aufhebung des Muskeltonus durch Kokain und Novokain (Nikotin-Kokain-Antagonismus). [**On the theory of muscular tone. I. The abolition of muscle tone by cocaine and novocaine. (The antagonism between nicotine and cocaine.)**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 149.

Frank, E., und **Stern, R.** II. Über den Angriffspunkt des Guanidins und Methylguanidins bei der Erzeugung motorischer Reizerscheinungen (Guanidin-Kokain-Antagonismus). [**II. The localization of the stimulus of guanidine and methylguanidine in the production of motor effects. (The antagonism between guanidine and cocaine.)**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 168.

It has been shown that intramuscular injections of cocaine can abolish the muscular spasm of tetanus, and the explanation which has been given is that cocaine paralyses the sensory terminations in the muscles themselves of the reflex arc which maintains normal tone. The first paper proves this explanation to be incorrect, for cocaine can abolish the spasm produced in the muscles of a frog by nicotine, three weeks after all the nerves to the muscles have been divided. The second paper shows that cocaine can abolish the twitchings produced in a frog by guanidine. Now guanidine application does not affect the excitability of an ordinary frog nerve-muscle preparation in response to break induction shocks, and its action is therefore referred to the receptive substance at the termination of the para-sympathetic (vagus) fibres which are considered (as distinct from the ordinary motor nerves) to be responsible for muscle tone. Cocaine therefore acts at the same point. J. H. B.

Loewy, O. Über humorale Übertragbarkeit der Herznervenwirkung. I. [**On the humoral transferability of the action of the cardiac nerves. I.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 239.

If the fluid with which a frog's heart is perfused is collected during a period over which the heart is inhibited by stimulation of the vagus, this perfusate will produce on a normal heart effects similar to those of vagus stimulation. Similarly, after stimulation of the accelerators (heart atropinized) the perfusate will cause acceleration of a normal heart. The author believes that inhibition and acceleration may be due to the production of specific substances. C. L. E.

Vorschütz, J. Ruhestrom und Durchlässigkeit. I. Untersuchungen mit Farbstoffen. [**Current of rest and permeability. I. Experiments with dyes.**] *Arch. f. d. ges. Physiol.*, 1921, **189**, 181.

It was shown by Beutner ('Die Entstehung elektrischer Ströme in lebenden Geweben und ihre künstliche Nachahmung durch synthetische organische Substanzen', Monograph publ. F. Enke, Stuttgart, 1920), that if two saline solutions of different composition are separated by a fluid which is immiscible with water, an electrical potential difference dependent on the solubilities of the ions on the two sides in the insoluble phase, is established. This suggests a connexion between the permeability of cells and the current of rest, on the basis of distribution of ions in a lipoid phase. The hypothesis was tested by studying the effect of acid and basic dyestuffs on the rest-current of muscle. All the basic dyes tested were lipoid-soluble, and all produced an electro-negative condition in the muscle, but this might have been due to injury: they accelerate sedimentation and agglutination of blood-corpuscles, which is also accepted by the author as an indication of some structural alteration. Some acid dyes engender an electro-negative condition, and these also injure the tissue. But 3 out of the 34 acid dyes examined caused an electro-positive state, and these three were also lipoid-soluble. These effects, when allowance is made for injury, lend some support to Beutner's theory that the boundary between 'oil' phase and a solution with an organic cation becomes negative, while if the anion is organic the boundary becomes positive. Echtrot *A* and *B* were two acid dyes producing positivity, soluble in lipoids, and not causing injury to the tissue. C. L. E.

Brewster, J. F. The use of edestin in determining the proteolytic activity of pepsin. *J. Biol. Chem.*, 1921, **46**, 119.

A description is given of a refined method of estimating pepsin by the use of edestin, the globulin of hemp seed. The edestin method was originally employed by Fuld and Levison. The author describes at length the method of obtaining standard edestin by recrystallization of the protein. The edestin content is calculated from the nitrogen content of the protein. R. A. P.

Langecker, H. Zur Fluoreszenzbeobachtung bei den Porphyrinen. [**On the fluorescence of the porphyrines.**] *Ztschr. f. physiol. Chem.*, 1921, **115**, 1.

It is found that the fluorescence of urines containing small amounts of porphyrin constitutes a slightly more delicate test than the spectroscopic method (absorption bands). Cases of phthisis, acute nephritis, disease of the liver, rheumatism, and conjunctivitis vernalis yielded urines rich in porphyrin, while the urine from a case of haemolytic icterus contained a particularly large quantity. H. W. D.

Langecker, H. Vergleichende Untersuchungen über die chemische Zusammensetzung von menschlichen Nägeln aus verschiedenen Lebensaltern. [**Comparative experiments on the chemical composition of human nails from subjects of various ages.**] *Ztschr. f. physiol. Chem.*, 1921, **115**, 38.

Chemical examination shows that human nails vary very little in composition with age or condition of health. H. W. D.

Lieb, H. Über die chemische Natur des bei der Luesreaktion nach Meinicke (D. M.) entstehenden Niederschlages. [**On the chemical nature of the precipitate obtained in Meinicke's (D. M.) lues reaction.**] *Ztschr. f. physiol. Chem.*, 1921, **115**, 147.

The results of micro-analyses of the precipitate show it to be composed mainly of lipoids derived from the alcoholic extract of horse's heart-muscle employed in the reaction. The precipitate contains very small amounts of cholesterin and adsorbed protein. H. W. D.

Schultz, E. W., and **Chandler, L. R.** **The acidity of goats' milk in terms of hydrogen-ion concentration, with comparisons to that of cows and human milk. The size of fat globules in goats' milk.** *J. Biol. Chem.*, 1921, **46**, 129.

In the first paper it is reported that goats' milk is slightly more acid than cows' milk and considerably more acid than human milk. It appears from the second paper that the fat in goats' milk is much more finely divided than that of human or cows' milk. This must mean that unless there is alteration in the size of the globules of fat as they pass through the stomach, goats' milk is more accessible to the activity of the fat splitting enzyme lipase than the other milks mentioned. R. A. P.

Voegtlin, C. **Recent work on pellagra.** *U.S. Public Health Reports*, 1920, **35**, 1435. (*Chem. Abstr.*, 1921, **15**, 1340.)

No direct proof has ever been brought forward that pellagra can be transmitted experimentally to man or to animals. Direct proof supports the hypothesis that a causal relation exists between pellagra and a restricted vegetable diet. In pellagra, definite changes from the normal metabolism occur and indicate decreased gastric secretion and increased intestinal putrefaction. Diet is the essential factor in the treatment and prevention of this disease; an appropriate change in diet suffices without any change in the other sanitary conditions. A diet of the composition used by pellagrins prior to their attack by the disease produces malnutrition and certain pathological changes similar to those occurring in pellagra. However, typical pellagrous dermatitis has not been observed in animals. Continued consumption of a restricted vegetable diet has produced pellagrous symptoms in man. While the nature of the dietary defect has not been discovered, certain observations point to a combined deficiency in some of the well-recognized dietary factors as the cause of the pellagrous syndrome. A bibliography of 46 references is appended to the article. C. G. L. W.

RADIOLOGY

Radiotechnique

Donnithorne, H. E., and **Baker, F. E.** **Pastilles and their colour measurement.** *Arch. Radiol. & Electroth.*, 1921, No. **246**, 239.

Barium platinocyanide tetrahydrate ($BaPt(CN)_64H_2O$) is the salt employed in the manufacture of the various brands of pastilles, whose colour change under X-ray bombardment furnishes a measure of the dosage. It exists in at least three forms, differing in crystalline structure, colour, and fluorescing power, and it is therefore important that standard conditions should be carefully maintained in the commercial preparation of the salt, so as to avoid the necessity for a fresh standard tint for each batch.

In the original method as devised by Drs. Sabouraud and Noiré the pastille was placed at 7·5 cm. distance from the target of the tube, and the skin at 15 cm. (the Sabouraud distance). In this position it was decided that the skin had received the maximum safe dose when the pastille had changed from the 'A' to the 'B' tint, in colour from yellow-green to a dull orange.

In modern practice, owing to the larger X-ray tubes employed, the pastille must often be placed further off, and the distance from target to skin has to be correspondingly increased. Radiometers have, however, been designed with a series of intermediate tints, by which the Sabouraud distance is retained and the change of colour of the pastille to some intermediate tint at another fixed distance still measures the same dosage. For example, with the pastille at 10·6 cm., the skin at 15 cm. receives twice the dose registered by the colour change. The radiometer is also used to measure fractional doses. The standard tints employed in matching the pastille should be free from any tendency to fade or change in colour, and the actual matching should always be done in the same light of the same intensity. B. D. W.

D'Halluin, M., et **Raquet, D.** Exploration radiologique du tube digestif. Une formule—un contrôle. [**The radiological examination of the digestive system.**] *Arch. d'électric. méd.*, 1921, **29**, 105.

Two types of preparation are used in the X-ray examination of the stomach and digestive system, the one 'bismuth milk' in which the salt of bismuth is in suspension in a mucilaginous solution, and the other 'the opaque meal' a semi-solid mixture of the bismuth or barium salt with a suitable food. The essential properties of the opaque meal are, that it should be easy to make, have a pleasant taste, and be perfectly innocuous. The authors have used for some years an 'emulsion powder' (*poudre de looch*) as a base for bismuth or barium meals. This preparation meets the above conditions and is not so gummy as some others in use.

The white or almond emulsion of the codex is composed of:

Sweet almonds	30	gm.
Bitter „	2	„
White sugar	0·3	„
Gum tragacanth (powdered) . . .	0·5	„
Orange-flower water	10	„
Water	120	„

An emulsion is made of the almonds, sugar, and water, and the gum and opaque powder ground up and added, the emulsion and orange-flower water added slowly with constant beating. This emulsion powder can be obtained commercially and then requires only the addition of water.

With regard to the particular opaque substance employed, bismuth carbonate neutralizes more or less the gastric juices, whilst barium sulphate tends to hasten the evacuation of the bowels. Bismuth sub-nitrate was abandoned as the cause of a number of accidents. It is very important that whatever salt is employed it should be in a high state of purity. The authors describe in detail their methods of testing samples of barium sulphate for traces of the heavy metals, and, what are often present, soluble salts of barium. B. D. W.

Radiodiagnosis

Japiot, P. La sacralisation de la cinquième vertèbre lombaire. [**Sacralization of the fifth lumbar vertebra.**] *J. de radiol. et d'électrol.*, 1921, **5,** 145.

Sacralization of the fifth lumbar vertebra is of importance because of the part it plays in lumbo-sacral neuralgias and sciatica of unknown cause; it is found in a considerable number of cases when care is taken to look for it. It may remain latent or may be revealed by a simple scoliosis, but more frequently gives rise to pain, usually when the subject is between 20 and 30 years old, generally as a result of trauma. The pain varies much in different subjects, and often simulates an affection of the urinary system. Some clinical signs may lead one to suspect the condition, but the X-rays are the only certain method of diagnosis. A description of the technique and the various normal appearances of the fifth lumbar vertebra are given; to obtain a correct image of the bone and its relations with the neighbouring bones it is necessary (1) to centre correctly on the vertebra and to place the pelvis as symmetrically as possible, and (2) to take several negatives in case of doubt from various angles of incidence. Between the normal and complete sacralization there are many stages: in many cases the radiologist can only point out abnormalities in the bone, but he can state that sacralization is present (1) when the transverse processes are clearly asymmetrical because of the hypertrophy of one of them, (2) when there is contact between the transverse process on the neighbouring bones. A description is given of the various ways in which sacralization can occur.

The diagnostic value of the radiograph. In some cases the X-ray plate aids diagnosis, but more often it is the only positive sign. It is of great use in eliminating Pott's disease of the lumbar vertebrae. The author then describes two of his cases.

Radiotherapy of painful sacralization. The Americans believe in a mechanical origin of the pain, and have practised resection with some benefit. The Italians believe more in irritation due to compression of the fifth lumbar nerve and traction on the corda equina, and have tried to act upon this latter part by radiotherapy. The author has treated four cases by radiotherapy with good and rapid results, which leads him to think that, although the treatment of this condition is in its early stages, radiotherapy should be continued. P. L.-B.

Liautard. Hoquet par contraction myoclonique isolée d'une hémicoupole diaphragmatique. [B.] [**Hiccough due to myoclonic contraction limited to one cupola of the diaphragm.**] *Arch. d'électric. méd. et de physiothérap.*, 1921, June, 183.

The author states that hiccough is due to a double spasm: the first expiratory and only revealed by graphic records, and the second inspiratory and accompanied by spasm of the glottis. Four types of hiccough are described: (1) neuropathic, (2) reflex, (3) as a complication of influenza and infectious diseases, (4) epidemic hiccough of central origin. Reference is made to the occurrence of hiccough in epidemic encephalitis; the author observed one of these cases under X-rays and showed that immediately before the myoclonus the diaphragmatic muscle was raised sharply on the right side and the ascent of the cupola was more marked; as soon as the noise of the hiccough was produced the right half of the diaphragm alone became flattened, lost its roundness, and remained contracted for several seconds with several minute contractions—true muscular spasm. The myoclonus was unilateral, as if the centre of the right phrenic nerve alone were affected. Faradization of the phrenic was practically without success.

P. L.-B.

TOUSEY, S. Dental infection in systemic diseases. Facts that our patients should know, with special reference to radiographic diagnosis. *Am. J. Electrotherap. & Radiol.*, 1921, **5**, 185.

The author enumerates a number of conditions in which dental infection has been proved to be the primary focus of infection. He points out that in some cases it is easy to find which is the offending tooth or teeth, but that in many cases radiographic examination alone gives a certain diagnosis. Another great advantage of radiographic examination is that it shows those teeth which are not infected, thus saving the patient from having all the teeth removed.

P. L.-B.

JAISSON, C. Étude radiologique de l'appendice dans l'appendicite chronique. [**The radiological study of the appendix in chronic appendicitis.**] [**B.**] *J. de radiol. et d'électrol.*, 1921, **5**, 256.

The author gives a short review of the past work done on the subject, and goes on to describe his technique for the study of the appendix, (*a*) in health, (*b*) in chronic appendicitis. A castor oil purge is not essential. After taking the meal—a description of which is given—a series of examinations is made every six hours, radioscopical to study the mobility and contractions of the appendix and the existence of tender points, and radiographical so as to have a permanent record. Three plates at least are taken.

Examination of the healthy appendix. The subject was aged 11 years. A description is given of the picture after 4, 8, 24, 28, and 32 hours. After 4 hours the appendix is beginning to fill, also the caecum: after 8 hours only the distal part of the appendix is empty: after 24 hours the distal part of the appendix is also filled. After 28 hours the appendix commences to empty, and after 32 hours only the distal portion contains any of the opaque meal. A description is also given of the shape and movements of the appendix during the examinations.

Examination of the appendix in chronic appendicitis. The radiographic characteristics are divided into physical and functional. (*a*) *Physical signs*: (1) Inequality of filling up; this may be due to transparent faecal concretions or to mucus. (2) Kinks are very frequent, probably due to adhesions. (3) Faecal concretions, must be diagnosed from ureteral calculi, phleboliths, &c. (4) Vacuoles. (*b*) *Functional signs*: (1) Mobility; in health the appendix is very mobile, but fixed by adhesions in the disease under consideration. (2) Contractions; some authors assert that there is a hypermotility, but the author fails to support this view. (3) Tender points; in some cases the finding of these is easy, but may give rise to difficulty; their localization is of great importance according to the author. The tender point may be localized or diffuse, and does not always correspond to MacBurney's point. (4) Late emptying; in some cases the meal remains in the appendix three days or more. In conclusion the author does not claim that radiological examination will solve all difficulties, but states that it is of great assistance in doubtful cases. P. L.-B.

Palmieri, G. Sur la possibilité de reconstruire le cœur du vivant en plastique à l'aide des rayons X. [**On the possibility of making a model of the heart of a living person with the aid of X-rays.**] *Réunion scientif.*, 1919, Aug. (*J. de radiol. et d'électrol.*, 1921, **5**, 185.)

The method consists of two phases: (1) Radioscopic tracings. (2) Plastic reconstruction.

I. The author's apparatus consists of an X-ray tube, a fluorescent screen placed at a distance of 80 cm. from the focus, and a movable armchair whose axis of rotation cuts the normal ray at 30 cm. from the screen and 50 cm. from the anode. Two threads perpendicular to one another are placed so that their point of intersection corresponds to the normal ray and indicates on the screen the central point of the tube. The patient occupies the chair—body straight, arms raised, and elbows bent forward. The author usually takes seven projections at an angular distance of 30° from one another: lateral right; oblique anterior right 60°; oblique anterior right 30°: right anterior; oblique anterior left 30°; oblique anterior left 60°; lateral left.

II. The cardiac images thus obtained are traced on, and cut out of cardboard. The cardboard figures are then used to mould a solid model in plaster by means of a simple instrument; a small table 80 cm. by 15 cm.; at each of the two extremities, an upright of about 20 cm.; and between the two a horizontal plate of 30 cm. diameter, movable on a vertical axis which is 30 cm. away from one of the two uprights and 50 cm. from the other; to this latter a wire thread is fixed and held in the operator's hand; to the other upright is fixed one of the figures cut out in cardboard, care being taken to make the point of incidence of the normal ray marked on each drawing coincide with the point under which one reckons the perpendicular from the point from which the metallic thread starts, will fall.

On the movable plate is placed a block of plaster; with the aid of the thread fixed at one end and held in the operator's hand by the other, the sinuosities of the cardboard which represents a cardiac projection are followed, and this thread, passing over the block of plaster cuts on it a shape in which is included the figure of the heart; After turning the plate 90° the operation is repeated, the thread being carried round the contour of the cardboard figure corresponding to this position.

By repeating the same operation for the different projections the author finally obtained an irregular solid, near enough to the shape of the heart that must be regarded as included therein. On the model presented were clearly to be seen, not only the mass of the heart, but also the aortic arch, pulmonary artery and its two main branches, the two auricles, the two venae cavae, &c., peculiarities which are certainly not obtainable when operating on a living person, but which demonstrate from the theoretical point of view, the accuracy and exactitude of the method.

The method gives the following information in cardiology:—

1. Exact (or nearly exact) determination of the cardiac volume.
2. Exact (or nearly exact) determination of the cardiac condition.
3. Exact localization of foreign bodies. S. U. L.-B.

PARTURIER, G., et **AIMARD, J.** Ulcus de la deuxième portion du duodénum. Contribution à la séméiologie objective clinique et radiologique basée sur dix-huit cas. [**Ulcer of the second part of the duodenum. Contribution to the objective clinical and radiological symptomatology based on eighteen cases.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **41**, 1667. (*J. de radiol. et d'électrol.*, 1921, **5**, 231.)

An important and very interesting contribution to the diagnosis of duodenal ulcer. From the radioscopic point of view the authors willingly allow the following formula:—hyperkinesia with rapid evacuation of a stomach in ptosis should lead one to consider the possibility of simple or ulcerative duodenitis, especially when there exists a painful point on the duodenum.

The authors have endeavoured by means of radiological examination, to fix a duodenal topography in relation to points as exact and invariable as possible. To this end they imagine an ideal umbilicus represented by the middle of the distance separating the iliac crests at their highest parts. From this ideal umbilicus they draw three lines of which the first ends at the 8th rib, the second at the antero-superior iliac spine, and the third at the anterior extremity of the 10th costal arch. Normally the first of these lines would meet the upper curve of the duodenum, the second would meet its lower curve, and the third, the part of the duodenum between the two curves. This third line, the most important, is the one which is valuable pathologically because it crosses the direction of the second portion of the duodenum more or less high up, according to the degree of ptosis or of elevation of the organ. The point of bisection which corresponds normally to the centre of this line is carried inwards in the case of ptosis, and then practically corresponds to the union of its internal third with its central third in the recumbent position. Pressure in the neighbourhood of this point will cause pain in cases of duodenitis, periduodenitis, or of ulcer.

According to the authors, duodenal ulcers most often assume the disguise of hepatic colic and especially of gall-bladder colic. Included in the number of signs they enumerate for differential diagnosis is the sensibility of the duodenal tract to pressure, determined by the method indicated, and especially the existence of a painful point on the line from ideal umbilicus to 10th rib. S. U. L.-B.

COLIEZ, R. Le pneumopéritoine artificiel (P. P.) en radiodiagnostic. [**Artificial pneumoperitoneum in radiodiagnosis.**] *Thèse de Par.*, 1920. (*J. de radiol. et d'électrol.*, 1921, **5**, 176.)

In Chapter I of his volume dealing with this subject the author shows the rôle played by the gaseous medium in obtaining radiological images. Chapter II recounts the history; Chapter III deals with technique. The digestive tract must be previously evacuated as completely as possible;

Kuss's apparatus for pneumothorax is used, but the communicating vases have a capacity of 2,000 c.cm., the trocar employed is that of Kuss, slightly modified, but the author gives us to understand that possibly, in the future a simple needle will be systematically used, as is already the practice of some authors. Introduction of the trocar is made three times, corresponding to the three anatomical planes; oblique puncture of the skin, puncture of the muscular plane (the trocar being now perpendicular) by separating the fibres rather than by pressure; puncture of the fascia transversalis whose resistance is overcome by continued pressure and whose puncture produces a sensation like the bursting of the skin of a drum. Injection should be slow and under slight pressure and continuously controlled by the manometer; too great pressure in this latter will show, either that insufflation is taking place unsatisfactorily, or that there exists an intraperitoneal septum. It is useless to continue insufflation until a previously-determined pressure has been obtained, for with patients whose skin is little-resisting, as much as 8 litres of gas may be injected, which is quite useless; with 2 litres visibility is very good.

Chapter IV contains criticism of the method and shows first that, since the trocar is not a bistouri and the mobile intestine offers no resistance to a gently manipulated trocar, perforation of a free part of the intestine is not possible. Haemorrhage need not be feared if puncture is made two finger's width above the umbilicus in the left rectus muscle at its external edge. Peritoneal infection can be avoided by the usual precautions of asepsis and by a sufficiently thick cotton-wool filter for the gas. It is not possible to produce dangerous over-pressure with this apparatus as it ceases to insufflate when pressure exceeds 20 cm. of water. The use of oxygen or carbonic acid gas will obviate gaseous embolism, since they are both easily fixed by haemoglobin. The only counter-indications are a very bad general condition hindering all prolonged examination; marked cardiac or respiratory affections; acute pathological conditions of the abdominal organs; recent adhesions which must be respected. The author estimates that, up to the present time, he has treated more than 1,500 cases in this way without accident.

Chapter V considers the results obtained; the abdomen rendered transparent, can be radioscopically examined, and after displacing the gaseous contents by changing the position of the patient, different organs are rendered visible. S. U. L.-B.

Barbarin, P. La maladie de Schlatter. [**Schlatter's disease.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1921, Nos. **2** and **3**. (*J. de radiol. et d'électrol.*, 1921, **5**, 227.)

'Schlatter's disease' is the name given to a lesion of the anterior epiphysis of the tibia. The most frequent form is found in growing children of from 13 to 15 years old. It is characterized by hypertrophy of this epiphysis, transient pain, slight and inconstant reaction on the lower part of the articulation, a benign course. Radiography reveals a sort of raising of one or both of the bony epiphyseal points. The author has always found in aetiology, a clear traumatism or several small repeated traumatisms, but has also found an inflammatory element; a slight attack of osteitis never, or rarely producing suppuration. He shows two radiographs: (1) Of a girl of 13, in which is seen the particular aspect of the tibial epiphysis noted by Schlatter; separation of the point of the lower tuberosity from the anterior face of the tibia. (2) Of a man of 45, who was affected with this lesion at the age of 13. In this case the successive inflammatory attacks could be distinguished by the irregularities of the surface of the bone. A separated bony nodule was present, which had moved little by little into the tendon. This nodule never became re-joined.

Radiography and development also help in diagnosis of the condition from a white tumour of the knee in its early stage.

Discussion. Lance thought that the causal traumatism referred to is often insignificant and is sometimes not present at all. The various radiological aspects can be found in subjects of the same age and often on a healthy knee, or may be reproduced if the member, instead of being placed exactly in profile during the taking of the plate, is in gradual rotation. In 17 cases of Schlatter's disease where intervention has been resorted to, no fractures or detached fragments were found.

Mouchet held that there is no such thing as Schlatter's disease, but there is an anterior tibial apophysitis in adolescents presenting variable clinical developments and variable radiographic images, often brought to light by an injury, but this appears to be only an osseous congestion due to development. S. U. L.-B.

Radiobiology

Mottram, J. C. The effect of increased protection from radiation upon the blood condition of radium workers. *Arch. Radiol. & Electroth.*, 1921, **25**, 368.

In 1920 the author published his findings upon the corpuscular content of the blood in workers in the Radium Institute, London. He described a profound leucopenia affecting both polynuclears and lymphocytes together with a mild anaemia accompanied by a high-colour index Since these investigations were made increased protection from irradiation was afforded the workers, and the present paper indicates the results after such increased protection had been in operation for six months. The observations bear upon 5 males and 5 females. In respect of red cells the blood count in all the females and two of the males had risen, and now presents approximately a median value which is regarded as 5·5 million for males and 4·9 million for females. In one male the value has risen slightly but is still low, and in the remaining two males a fall has occurred which may be partially explicable on other grounds. In respect of polynuclear cells the five lowest original counts show considerable approaches towards the normal, and the two lowest lymphocyte counts also show a rise, otherwise little change is noted in the leucocytic counts. The actual protective devices employed consist in protection from emanation, improved ventilation of the rooms, manipulation of emanation applicators before the active deposit has been fully formed, use of long-handled wooden forceps, diminished handling of the applicators during transit and in actual clinical use, leather lined lead rubber gloves. In the screening of applicators and against gamma radiation generally temporary workers are used as far as possible. The lead screens on the tables and those behind which the manipulations are carried out are 5 cm. thick. Due instruction is also given the workers as to how advantage may be taken of these protective devices. W. S. L.-B.

Auer, J., and **Witherbee, W. D. Studies on decreasing the reaction of normal skin to destructive doses of X-rays by pharmacological means and on the mechanism involved.** *J. Exper. M.*, 1921, **33**, 791.

Arising out of a previous investigation in which it was shown that an organism sensitized by a foreign protein can locally auto-inoculate itself with the same protein under certain conditions, the authors carried out experiments on rabbits and used X-rays as the irritating agent. The essential plan of the investigation was to determine whether the skin of the rabbit's ear when exposed to a constant degree of powerfully damaging X-radiation reacted in different ways according as the animal was (1) previously untreated, (2) injected with horse-serum after irradiation, (3) sensitized with horse-serum previous to irradiation, (4) sensitized with horse-serum before irradiation and also injected therewith subsequent to irradiation. Full details of the methods are given in the paper. Here it may be mentioned that a Coolidge tube was used, spark gap 3 inches, 10 ma. current, 6 inches distance from the target, 20 minutes exposure, no filtration beyond a thin layer of cardboard. The seat of irradiation was an area 2 × 2 cm. on the ear, and the rest of the animal was rigorously shielded with lead. The horse-serum was injected (10 c.cm.) intraperitoneally 13 days after irradiation in the serum control, and sensitized-reinjected groups, and for sensitization 1 c.cm. was injected subcutaneously or intramuscularly on 4 occasions, at 3–4 days' intervals, 10 days before irradiation. It was found that a great difference from the other animals was obtained in the sensitized group, for whereas the others invariably showed local gangrene and definite perforation of the ear the sensitized group showed great delay in these changes or they were absent altogether (photographs). The reaction to the irritant when serum had been injected showed itself in two inflammatory stages, the first being mildly acute, superficial, epilatory and pigmentary, and coming on within 4 days, the second being separated from the first by an interval, subacute, and followed by dry gangrene. In normal animals the first inflammatory stage passed directly into gangrene. The authors point out that 'it is possible that the procedure of increasing the resistance of the skin to a destructive dose of X-rays by means of a previous sensitization with protein may be applicable in the treatment of certain types of inoperable disease, when it is important to use massive doses of X-rays'. The most obvious criticism is the small number of animals employed in the investigation, 5 rabbits only being used in each group (20 animals in all). A further criticism is that although the X-rays were given in a strongly damaging dose it is not certain—owing to the known variability of even the Coolidge tube while running—that all the animals received absolutely the same dose. Nevertheless, the paper is one of great importance, and will repay careful study. W. S. L.-B.

Pech, J.-L. (1). Les différences de potentiel en biologie. [**Differences of potential in biology.**] *Presse méd.*, 1921, Jan. 1. (*J. de radiol. et d'électrol.*, 1921, **5**, 238.)

Pech, J.-L. (**2**). Les radiations en biologie. [**Radiations in biology.**] *Presse méd.*, 1921, Jan. 5 and 19. (*J. de radiol. et d'électrol.*, 1921, **5**, 224.)

Following various experimental facts the author puts forward these four general rules:

(1) Living beings appear especially sensible to weak and continued

electric variations of the surrounding medium when this is less conducting than they.

(2) Living beings, as conductors, are not comparable with simple electrolytic solutions, but rather with a series of varied and complex solutions from one another by more or less permeable walls.

(3) The differences of potential between organized tissues and liquids in contact (even circulating blood in living beings) can be modified under the action of certain physical or chemical agents or of certain organic products.

(4) The variations in difference of potential between a tissue and a liquid or a fluid in contact may modify the osmotic changes.

These ideas may furnish medicine and physiology with the explanation of a certain number of phenomena. Thus it is that the action of various radiations (X-rays, luminous rays of the solar spectrum, ultra-violet rays, &c.) on living beings may be explained by the production of different photoelectric phenomena according to different cells, whence, modification of the difference of potential between these cells, that is to say, modification of the physico-chemical changes, affecting the nutrition of the tissues and the functioning of the organism.

The difference of intercellular potential may also explain the biological action of substances which react to extremely weak doses without producing any appreciable modifications on the tissues or tissue fluids.

S. U. L.-B.

Radium Therapy

Regaud, C., Roux-Berger, J., Lacanague, A., Cerbron, H., Coutard, H., et Richard, G. Sur la technique de la Curiethérapie dans le cancer du col de l'utérus. [**The technique of radium therapy in cancer of the cervix.**] *Bull. de l'Ass. franç. p. l'étude du cancer*, 1920, **7**, 224. (*J. de radiol. et d'électrol.*, 1921, **5**, 234.)

This important work rests on 150 cases observed for 15 months, studied from the anatomico-clinical, radiological, and histological points of view. From the outset the authors insist on the fact that their results are by no means final, and that their proposed technique calls for modification. In their researches they have used principally the uterine and vaginal capsules, since in practice they are the most important.

Uterine capsules. The use of the uterine canal is excellent since it is nearly central with regard to the surrounding tissue: further, the uterus allows a dosage which otherwise would produce severe lesions, without apparent harm. When the uterine canal is patent the technique is relatively easy. The object is to place a capsule throughout the length of the uterine canal so as to attack in some degree the lesions which may develop in the fundus. The radiation should be made homogeneous by means of a heavy filter; to do away with the soft secondary rays a double envelope of rubber 1 to 2 mm. thick is used, inside which is a sheath of aluminium 0·1 to 0·2 mm. thick. The radium-containing tubes being introduced into the bougie prepared as described, the open end is closed by cotton-wool, the position of the contents is marked with two knots of white wire, the apparatus is sterilized with iodine and then with alcohol and placed in position after dilating the cervix if necessary. When the cervical canal is obliterated and the uterine canal not patent, treatment is divided into two: first an apparatus like that used in vaginal capsules is placed in the cavity resulting from the destruction of the canal, in about a fortnight the surface of the uterus is clean and regular, it has become possible to douche the uterine canal, and at a second sitting treatment is carried out as above. A third eventuality must be considered, namely, hyperplasia of the cervix: the procedure is then either the use of needles or of Janeway's bare tubes for radiopuncture of the neoplastic mass. The disappearance of the mass will be made easier by curettage or better by removing each day the slough that is visible. After cicatrization the uterine canal is accessible and treatment is carried out as above.

Vaginal capsules. Radium burns of the vaginal mucous membrane should be absolutely avoided. The first filter is 2 mm. of platinum or 2·5 mm. of gold: the second is made of a double envelope of aluminium 0·1 to 0·2 mm. and by a second envelope of cork 5 mm. thick, immersed in paraffin. (*a*) *Positions of election.* There are, apart from the precervical position, those which can be obtained by depressing the lateral fornices so as to bring together the mucous membrane of the pelvic wall for 1·5 to 2 cm. These are the typical positions in early cervico-uterine cancer. To maintain the capsules in the lateral fornices, the authors use a colpostat made of a flexible spring enclosed in rubber, to the ends of which the cork filters are firmly attached. The application is completed by a plug of gauze, exactly filling the space, being placed between the cervix and the concavity of the spring, thus preventing displacement of the uterine tube. (*b*) *Positions of necessity.* These are those which have to be used when the positions of election are impractible or when the lesions have spread on to the vaginal wall. Isolated vaginal capsules in a sheath of wax are used and kept against the cervix with oiled gauze. Under these conditions sterilization of the parametrium, and the risks of injury to bladder or rectum should not be forgotten.

Doses, intensity, duration of irradiation, general lines of treatment. Several kinds of cure must be distinguished: the authors divide them into (1) Radium therapy as a cure; (2) as a palliative; (3) in cases of post-operative recurrence; (4) cases where the use of radium is doubtful or contra-indicated.

Accidents, complications, and sequelae of radium therapy. As regards accidents the authors mention perforations and burns, both due to insufficient filtration: the sequelae mentioned are retractions and stenoses, and the effects of irradiation on healthy tissues.

The authors prefer radium tubes to emanation tubes and believe that radium therapy alone can cure cases of cancer of the neck of the uterus when not too advanced. They insist on the importance of determining in each case the 'coefficient technique'. P. L.-B.

Rénou et **Degrais.** Résultats éloignés de la Curiethérapie de la leucémie myéloïde. - Valeur de la méthode et conduite de la cure. [**The late results in cases of myeloid leukemia treated by radium. The value of the method and the mode of treatment.**] *Bull. Acad. de méd.*, 1921, February, 207. (*Arch. d'électric. méd.*, 1921, **29**, 93.)

Since 1910 the authors have treated eight cases of myeloid leukaemia by applications of radium over the spleen.

For the most part the treatment was effected by means of thirteen flat applicators carrying 189 mgm. of bromide of radium, i. e. 101 mgm. of radium element. The superficial area of the entire apparatus was 244 sq. cm. indicating a mean intensity of 2·4 mgm. of radium element per sq. cm. of radiant surface. A filter of 2 mm. lead and 1 cm. gauze was used. A series of exposures for treatment lasted 48 hours and its value was 4,848 mgm.-hours. The patients died at intervals varying between two months and six years and a half after treatment was begun. The immediate effects were remarkable. Spleens which had occupied the whole abdominal cavity diminished rapidly in size from day to day until their normal volume was reached. The numbers of white cells fell from 320,000 to 70,000, then to 20,000 and even less. Myelocytes disappeared. The general condition of the patients improved, fever disappeared, weight increased, and strength was rapidly regained. Two of the patients became pregnant, and one of these was brought to term; her child showed no myelocytes in the blood, and is now nearly six years old.

After four to six weeks of treatment, the patients presented an illusion of cure, but when treatment was stopped, signs of the disease reappeared. On recommencement of the applications, the action was not the same, the cells having become accustomed to the radium rays. Finally at varying periods no action at all was produced, and the patients died. One patient lived 6½ years after the first of 25 applications. When she first came under treatment she was cachectic and almost dying; she became pregnant, but the confinement took place prematurely at five months.

The pathogenesis of this progressive radio-resistance of the myelocytes is yet to be determined. It may be that they become simply tolerant of the rays or it may be that, because of the fibrous transformation of the leukaemic spleen under influence of the rays, the destructive action of radium and X-rays (whose effect is almost analogous), on the myelocytes is hindered by this fibrous meshwork. Relapse took place more rapidly in the cases previously and frequently treated by X-rays and in those treated by closely repeated doses of radium. Contrary to the opinions held by them seven years ago, the authors now think that irradiations should be less frequent, but as intense as possible. The action of X-rays on the bone-marrow may also have beneficial effects in myeloid leukaemia. S. U. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

LETHARGIC ENCEPHALITIS

Classification. Cruchet (1) states that the condition described in May 1917 by Economo in Vienna, and in March 1918 by Netter in Paris, under the name of ‘lethargic encephalitis’, had already been isolated by him in April 1917 as one of the forms of subacute or diffuse encephalomyelitis. He describes the following nine forms of this disease, for which he prefers the term ‘epidemic encephalomyelitis’ or ‘Cruchet’s disease’, as it is known in the Bordeaux district: (1) mental form, characterized by cerebral torpor, disorientation, tremor, dysarthria, and changes in the cerebrospinal fluid suggesting general paralysis or some other form of dementia; (2) convulsive form; (3) choreic form; (4) meningeal form; (5) hemiplegic form; (6) ponto-cerebellar form; (7) bulbo-pontine form; (8) acute ataxic form; (9) anterior poliomyelitic form, a rare variety resembling infantile paralysis.

Aetiology. The portal of entry of infection is not yet determined. Dopter maintains that the virus penetrates the system by the nasopharynx, from which it is conveyed to the central nervous system, and that it is by the nasopharynx that it is eliminated, giving rise to a specific rhinopharyngitis, which in some abortive cases may be the only evidence of the disease. Netter, on the other hand, who attaches considerable aetiological importance to the salivary glands, states that the rhinopharyngitis described by Dopter is exceptional, as it was only in rare cases that he had been able to find a trace of a sore throat or even a slight catarrh preceding the appearance of nervous symptoms.

According to Netter (1), who treated 177 cases between November 1, 1919, and October 31, 1920, the disease started in more than half the cases in December, January, and February, and in less than a seventh in June, July, August, September, October, and November. This seasonal incidence of encephalitis is in striking contrast with poliomyelitis, whose maximum incidence is reached in July, August, and September.

Dunn and Heagey, of Omaha, who have collected 115 American cases, including 15 personal ones, found that 36 had a history of a respiratory infection within a year prior to the onset of encephalitis, the average time being two months. Among their personal cases 5 gave a history of repeated severe tonsil infections, 2 had had typhoid, 2 diphtheria, 2 inflammatory rheumatism, 1 scarlet fever, 1 chorea, 1 pleurisy, and 1 tuberculosis of the knee.

Lépine states that apart from influenza, which is a frequent but inconstant precursor, the principal aetiological factors of infective encephalitis are as follows: (1) Constitutional or at least old-standing nervous debility, excessive emotivity or excitability, and occasionally a definite history of insanity or organic cerebral disease. (2) Habitual and pronounced tendency to migraine. (3) Recent and prolonged strain, especially when associated with intense anguish and insomnia, as in a bombardment. (4) Habitual tendency to congestion or a definite congestive episode, such as sunstroke after bathing in a river. (5) Some episode in the genital life of women, such as menstruation or the menopause. Lépine concludes that the reason of epidemic encephalitis being so slightly contagious is that special conditions of receptivity are indispensable.

The importance of a nervous predisposition in the aetiology of lethargic encephalitis is also emphasized by Netter (2), Marañon, and Moncalvi.

Palitzsch compares the relations between lethargic encephalitis and influenza with those between general paralysis and syphilis, and maintains that a certain individual predisposition is required to develop encephalitis; 27 cases studied by him showed an abnormal irritability and marked susceptibility of the nervous system which was due to various causes. 8 had a well-marked neuropathic disposition which had previously given rise to nervous symptoms; 4 were syphilitic; 2 were heavy smokers; 1 had had a severe blow on the head three years previously, and was still suffering from the effects; 2 had undergone intense professional strain; and 4 had had severe articular rheumatism, so that there were only 6 who had not some nervous taint, and even these had been subjected to very hard work.

Cases of contagion in lethargic encephalitis are generally admitted to be rare. In a communication to the Société médicale des hôpitaux de Paris, on July 16, 1920, Netter (2) stated that among the 174 cases of lethargic encephalitis which he had seen since March 1918 only eight, or 4·6 per cent., were obviously connected with other cases of the disease. Three of these cases belonged to the same family, and two were children living in the same institution. Other examples of contagion have been reported by Claude and De Laulerie, Guillain and Lechelle (1), Lévy, De Laroche, Salvetti, Lemierre, and Roger and Blanchard. Netter (1), who thinks that the contagion is probably conveyed by the saliva, states that the disease may also be transmitted by convalescents, by persons with abortive or larval attacks, and even by healthy persons who have been near the patient. The possibility of the spread of the disease by healthy carriers is also maintained by Guillain and Lechelle (1), Roger and Blanchard, and Lemierre. On the other hand, Umber declares that lethargic encephalitis is not contagious, as he has treated all his cases in the general wards without any other patients or any members of the staff contracting the disease. How careful one should be in interpreting supposed cases of contagion he illustrates by the following case. A woman who died of typical lethargic encephalitis, confirmed by autopsy, had four weeks previously lost her child, aged six, from encephalitis, who had slept in the same bed with her. The autopsy on the child, however, showed that the encephalitis was secondary to streptococcal endopericarditis.

Delaunay, director of the Poitiers Medical School, suggests that lethargic encephalitis is a form of rabies on the following grounds. (1) In both cases the disease shows a predilection for the nervous system in spite of its protean character. (2) The microbial agent of lethargic encephalitis presents striking analogies to that of rabies. In both cases it is a filterable virus localized in the nerve centres, where it may remain latent a considerable time, as is shown by the long incubation period and the occurrence of relapses after apparent recovery. (3) In both affections the monkey is not very sensitive to the action of the virus, but the activity of the virus may be exalted by making it pass through the rabbit. (4) The specific virus of both affections is eliminated by the saliva. In ordinary years and *a fortiori* in 1920, when rabies in domestic animals was unusually prevalent, man was often contaminated either by licking or by food (meat and milk). Owing to the very small quantities of virus introduced under these conditions the virus remained latent, and finally disappeared without the disease becoming manifest. In 1920, as the result of unknown influences, possibly certain forms of influenza, the human organism became sensitized or anaphylactic, and the virus of rabies which had been lying latent in the nerve centres was roused into fresh activity.

Epidemiology. According to Netter (1) during 1919–20 not a single country in Europe escaped a visitation of the disease. All the departments of France were invaded, villages and towns alike. The disease also occurred in Spain, Portugal, Belgium, Holland, Switzerland, Denmark, Norway, Sweden, Finland, Poland, Roumania, and Bulgaria. Cases were reported in Palestine, India, Japan, Egypt, Morocco, French West Africa, Canada, Mexico, Uruguay, Brazil, the Argentine, Peru, the Malay Archipelago, the Philippines, and New Zealand.

Bernard and Renault report the results of an inquiry instituted by the French Ministry of Health as to the prevalence of lethargic encephalitis in France. 464 cases, including 10 doubtful ones, were reported between January 1 and May 1, 1920. 70 cases were reported in January, 206 in February, 144 in March, and 44 in April. 118 deaths were certified—a mortality of about 30 per cent. The prognosis would therefore appear to be very grave, but probably many mild cases were not reported. Adults were affected twice as frequently as children, but the average mortality was exactly the same in both periods of life. Although the disease did not assume the character of an intense epidemic in any part of France, there was no doubt as to its epidemic character, as in the period of four months and in 55 departments 464 cases were reported of a disease which had formerly only existed in a sporadic form. The idea of a possible relationship between lethargic encephalitis and poliomyelitis, which had been suggested in some medical societies, was not confirmed by the inquiry, for the reports received were unanimous in excluding any relationship between the two affections, and emphasized the absence of simultaneous cases of poliomyelitis and encephalitis. On the other hand, in 49 of the 55 departments which made a return the possibility of a close relationship between influenza and encephalitis was noted.

As the result of an inquiry into the prevalence of epidemic encephalomyelitis in the Bordeaux region Cruchet (2) found that 145 cases occurred there between March 1918 and October 1920. Their classification was as follows: meningo-encephalitic form, 56 cases; pontine and bulbo-pontine forms, 32 cases; choreic and myoclonic forms, 15 cases; mental form, 14 cases; epileptic form, 2 cases; hemiplegic form, 2 cases; cerebellar form, 1 case; spinal form, 6 cases; polyneuritic form, 3 cases; unclassified, 14 cases. Of the 145 cases, 27 died, a mortality of 18·6 per cent. But although recovery was frequent it was far from being always complete, and convalescence was extremely slow. The prognosis in the myoclonic form was usually grave. No cases of contagion were observed. There was no evidence to justify the conclusion that there was any constant relationship between epidemic encephalomyelitis and influenza, or between encephalomyelitis and acute poliomyelitis. The disease was observed in both sexes, in childhood and in adult life, but after 40 cases were rare.

According to Marañon lethargic encephalitis appeared in Spain at the beginning of the winter of 1919–20 at the same time as it did in France, thus coinciding with the end of the influenza epidemic. The disease spread very rapidly, for epidemic foci were reported almost simultaneously in all the provinces of Spain, the largest outbreak being in Valencia, where more than 100 cases were reported. No definite case of contagion was observed. The mortality was relatively low, being only 10 per cent. in Valencia and also at Madrid, in contrast with a mortality of 45 per cent. reported by Re at Naples and 25 per cent. in French statistics.

As the result of inquiries addressed to 265 medical men, 110 of whom replied, Kayser-Petersen comes to the following conclusions with regard to the epidemiology of epidemic encephalitis in Germany: (1) There is an extraordinarily close connexion between the occurrence of encephalitis and influenza, in that encephalitis in epidemic form only occurred in Germany shortly before, simultaneously with, or directly after an epidemic of influenza. (2) The time of appearance of encephalitis in the various districts of Germany varied considerably. (*a*) Isolated cases of encephalitis with the typical symptoms of epidemic encephalitis, such as lethargy and ocular palsies, have been observed all over Germany for years, especially in the large towns. (*b*) The first epidemic appearance of encephalitis in Germany took place at Kiel and Hamburg in the spring of 1918, and from the summer of 1918 to the winter of 1918–19, somewhat later at Stuttgart, from December 1918 to the summer of 1919, and later still in Munich, from January 1919 to the summer of 1919. (*c*) The second epidemic appearance of encephalitis began in December 1919, apparently simultaneously and independently in various districts, viz. in the Ruhr (Dortmund, Mühlheim, Barmen) and on the Rhine (Cologne) as well as at Danzig. The epidemic spread slowly during the first few months of 1920, so that by the end of the winter the principal parts of Germany had been affected. In Western Germany there was a definite advance of the disease from the north to the south and from the east to the west. (*d*) It was a remarkable fact that in numerous places no cases of encephalitis occurred at all, e. g. at Allenstein, Altenburg, Bremerhaven, Ingoldstadt, Wilhelmshaven, &c.

From observations made in Feb. 1921 in some villages in Lapland where lethargic encephalitis was very prevalent, Kling and Liljenquist, of Stockholm, found that in addition to typical cases there were a very large number of mild forms. The morbidity ranged from 7·1 to 45 per cent. In some families several members contracted the disease simultaneously, and in two houses almost all the inhabitants were affected. Side by side with severe cases presenting a typical clinical picture were others in whom the symptoms were less pronounced, and consisted of catarrh of the upper respiratory tract, insomnia, fever, headache, dilated and sluggish pupils, dissociation of the ocular movements and occasionally facial paresis. Some patients were subject to obstinate hiccough. There were also milder cases still, with the same catarrhal symptoms but without any signs of cerebral involvement. The writers' investigations showed nothing to justify the belief that lethargic encephalitis can be transmitted by water, milk, bugs, fleas, and lice. Dogs and cats which were examined showed no evidence of the disease.

Smith, of the United States Public Health Service, states that from September 1918 to May 1919 255 cases were reported for the entire United

States. The peak of the epidemic in New York City was reached during January, in Virginia during February, and in Louisiana, Illinois, and Texas during March. The largest number of cases for California was recorded during April, which, taken in conjunction with the foregoing, shows a gradual extension of the disease from east to west. Approximately 900 persons were exposed in the immediate families of the cases reported, and no secondary cases could be discovered. The case mortality was 29 per cent. for all cases and 60 per cent. for cases with a sudden onset.

Pathology. The material examined by Harbitz consisted of three cases of lethargic encephalitis, diagnosed as such before death. They occurred late in 1919 and early in 1920. The macroscopic appearance of the central nervous system was in every case practically normal. Microscopically, there were striking and, in Harbitz's experience, unique changes; from the cervical section of the cord to the posterior parts of the central ganglia there were diffuse inflammatory changes, affecting mainly the grey matter, but here and there the white also. These changes were most marked in the neighbourhood of the blood-vessels, but there was also a diffuse distribution of the disease, with infiltration of numerous nerve-cells and of the grey matter. Harbitz amplifies his description with six illustrations, and discusses seriatim the points identifying this disease with, or distinguishing it from, other acute infectious diseases of the central nervous system. His own investigations and his study of the literature incline him towards the belief that lethargic encephalitis is a disease *sui generis*. He suggests that the coincidence of lethargic encephalitis with outbreaks of influenza ever since the epidemic of 1890 may be due to 'activation' of the virus of the former by the latter in the same way that this appears to 'activate' streptococci and pneumococci, possibly also tubercle bacilli. In two of his cases small Gram-positive diplococci were found in smears from the central ganglia and the centrum semiovale. They were grown in pure culture on ascites-agar, forming small, transparent colonies which soon died out on subculture. Harbitz is dubious as to the importance of these bacteriological findings, observing that the bacteriology of acute poliomyelitis and other diseases of the central nervous system is a field in which it is easy to go astray.

Symptomatology. De Massary and Boulin reported on December 10, 1920, to the Société médicale des hôpitaux de Paris two cases in women, aged 22 and 57, in whom the disease assumed a *chronic course* with successive exacerbations. The first patient died after an illness of nine months, and the second patient was still alive thirteen months after the onset. In the subsequent discussion Sicard alluded to similar cases which he had seen, and Netter described the case of a girl whom he had diagnosed as suffering from lethargic encephalitis in March 1918, and had kept under observation since. Although her ocular symptoms cleared up the tremors persisted, and two and a half years after the onset she had another attack of diplopia, which was found by Morax to be due to paralysis of the third nerve without disturbance of accommodation or nystagmiform jerkings.

Turrettini and Piotrowski, of the Geneva Medical Clinic, who also report a case of nine months' duration, allude to two similar cases reported by Economo in which the disease lasted two years and eight months respectively. They remark that a very prolonged course is peculiar to the lethargic form, as it has never been observed in the myoclonic or other forms of epidemic encephalitis.

Gelma, of Strasbourg, draws attention to the occurrence of *sialorrhoea*, especially in the chronic forms of lethargic encephalitis. It appears at the onset of the disease and lasts for weeks or months. It is commoner in children than in adults, and is specially frequent between the ages of 13 and 20. It is sometimes accompanied by chronic coryza. It may be noted that Delater, in the description of his own attack, refers to his excessive salivation. Happ and Mason state that in their experience salivation usually comes late in the disease, and is frequently more marked at night than in the day-time. In this connexion reference may be made to the tender swelling of the parotids resembling mumps reported in the course of lethargic encephalitis by Lesné and Langle, Netter, Cesari and Durand, and Babonneix and Hubac. These writers refer to the fatal diseases in children described by Gordon in 1913 associated with acute interstitial parotitis which has since been identified with acute encephalitis. In the fatal case described by Netter and his assistants inoculation of the salivary glands into rabbits proved virulent.

Briand and Rouquier reported a case of severe lethargic encephalitis to the Société médicale des hôpitaux de Paris on June 4, 1920, in an airman, aged 30, complicated by *polyuria and polydipsia*, nearly 5½ litres of urine being passed in the 24 hours. In the subsequent discussion Dopter related a case complicated by a transient polyuria of 2½ to 3 litres a day. Hoke also describes a case of polyuria in a nurse, aged 23, suffering from lethargic encephalitis of the myoclonic type, who passed as much as 8 to 10 litres in the 24 hours. After injection of pituitary extract the amount of urine dropped to 3 litres. Apart from motor restlessness, examination of the nervous system was negative.

Frugoni calls attention to the existence of exceptional cases in which there is an appreciable *enlargement of the spleen* which, owing to its gradual development in the course of the diseases and the negative results of laboratory tests, appears to be due to lethargic encephalitis. He concludes that while the spleen in lethargic encephalitis is not generally affected the presence of a splenic tumour is not sufficient to exclude that disease.

In a communication to the Société médicale des hôpitaux de Paris on May 6, 1921, Livet reported four cases of *obesity* following lethargic encephalitis. Two of the patients were males and two females, their ages ranging from 16 to 43. He attributes the phenomenon to involvement of certain glands of internal secretion, especially the hypophysis, and possibly the thyroid and genital glands, and suggests that opotherapy should form part of the treatment of lethargic encephalitis. In the subsequent discussion Netter remarked that obesity was not a frequent complication of lethargic encephalitis, as he had seen it in only three instances out of 150 cases of lethargic encephalitis which he had kept under observation for a period varying from three months to three years. At a later meeting Nobécourt reported a case of a girl, aged 12½, who developed well-marked obesity in the eighth month of a subacute attack.

Obstinate *insomnia* as a symptom or sequel of lethargic encephalitis, especially in children, but also occurring in adults, has been described by numerous writers, such as Findlay and Shiskin, and Fletcher and Rolleston in Great Britain; Happ and Blackfan in the United States; Hofstadt, Pfaundler, Janecke, and Walter in Germany; Progulski and Gröbel in Austria; Reh and Rütimeyer in Switzerland; and Francioni, Roasenda, and Zalla in Italy. The characteristic feature of the insomnia is its persistence for months unaffected by treatment of any kind. In many of the cases the attack of lethargic encephalitis had been so slight as to have escaped recognition, and the insomnia was the first thing to attract attention, just as the occurrence of nephritis, cervical adenitis, or diarrhoea may be the first indication of scarlatinal infection.

Mayer, a Munich neurologist, who attributes the insomnia to irritation of the basal ganglia, states that many of the patients finally become suicidal, so that it is unsafe to leave them without supervision.

Pilcz, of Vienna, records a hitherto undescribed symptom of epidemic encephalitis, namely, *exaggeration of the sexual impulse* leading to masturbation in a woman aged 43, who had hitherto been of a cold disposition. Death took place at the end of the fourth week of disease, six days after the appearance of the symptom, which lasted only a few days. No autopsy was performed, but owing to the absence of the knee-jerk on one side and its diminution on the other, Pilcz is inclined to regard the sexual excitement as of spinal origin, especially as psychical or cerebral symptoms were not pronounced at the time. On the other hand, diminution of the sexual appetite, both in men and women, as a sequel of epidemic encephalitis is mentioned by Hess and Sabrazès.

Happ and Mason frequently observed *enuresis nocturna* in children following recovery from the disease.

Numerous writers, such as Hesnard, Petit, Todde, Bosc, Eschbach and Matet, Widal, May and Chevalley, Ardin-Deltheil, Raymond and Derrieu, and Leahy and Sands, discuss the frequency and importance of the *mental complications* and sequelae of lethargic encephalitis. Hesnard, who regards the psychical symptoms as next in frequency to drowsiness and ophthalmoplegia, remarks that while there is nothing rigorously specific in the mental state, retardation of the psychical processes and pseudo-Parkinsonian catatonia are characteristic of lethargic encephalitis. Hesnard emphasizes the likelihood of incomplete recovery, with the result that a more or less profound dementia develops. In addition to the acute and subacute mental forms of epidemic encephalitis, Petit describes a form characterized by an abnormally long course which is sometimes interrupted by remissions or intermissions. He records three illustrative cases in which various psychopathic syndromes, such as acute delirium, mental confusion, hallucinatory delirium, obsessions, and phobias persisted continuously or with remissions or intermissions for more than a year. Todde, of Cagliari, who records two fatal cases, remarks that during the last epidemic, in contrast with previous ones, there was a predominance of cases with mental symptoms and almost entire absence of cranial nerve manifestations. Widal, May, and Chevalley report a case resembling dementia praecox, but ending in complete recovery.

Three cases of the ambulant form of lethargic encephalitis with symptoms resembling the onset of general paralysis are described by Ardin-Deltheil, Raymond and Derrieu. During the epidemic of lethargic encephalitis at Montpellier, Bosc found that delirium was the most constant symptom. It was sometimes accompanied by a number of other phenomena, sometimes by somnolence alone, and in four cases, some of which were apyrexial and others febrile, it was the only manifestation of the disease. Leahy and Sands report six cases of mental disorder in children aged from 5 to 14½ years following epidemic encephalitis and characterized by purposeless impulsive motor acts, marked irritability, definite attention disorders, distractibility and changing, variable moods, inadequate and inconsistent emotional reactions, marked insomnia, precocious sexual feeling, and intense eroticism.

Sicard records three cases in which epidemic encephalitis complicated *pre-existing diseases,* viz. tabes, exophthalmic goitre, and duodenal ulcer respectively. In the first two cases the encephalitis, which was of a relatively mild character, did not produce any unfavourable effect upon the pre-existing disease, while in the third case the duodenal ulcer was possibly unfavourably influenced by the encephalitis, though this was impossible to prove.

The occurrence of *lethargic encephalitis in children,* though less frequent than in adults, has formed the subject of papers by Findlay and Shiskin, Zweigenthal, and Stadelmann. Zweigenthal, who has observed 40 cases at the Brunn Children's Clinic, divides them into three groups, viz. choreiform, lethargic, and mixed. The first group, which is the commonest in children, comprised 20 cases, 17 of which were under 10 years of age. 9 cases belonged to the second group and 9 to the third. Two cases were placed by themselves in which epileptoid and hysterical convulsions with neuralgic symptoms were the principal features. In the great majority of cases the disease assumed a prolonged course. Zweigenthal considers that the most constant symptoms of epidemic encephalitis in children are insomnia at the onset, increase of restlessness at night, persistence of choreiform movements during sleep, which served to distinguish the condition from true chorea, and anomalies of the pulse such as tachycardia and bradycardia.

Stadelmann, of the Frankfort University Children's Clinic, attributes the comparative rarity of cases in children to the difficulty in diagnosing the disease at this time of life. Apart from convulsions, which dominate the clinical picture in infancy and may also occur in many other toxi-infective processes, the symptoms may be so ill-marked that it is only after long and careful observation that any deviations from the normal can be found. Stadelmann records his observations on 20 cases in children up to the age of 14 observed between December 1919 and June 1920, and on 15 cases seen between 1912 and 1919. Affection of the respiratory centre was a frequent cause of death. With few exceptions paralyses occurring during the acute stage completely cleared up. Some cases ended in dementia.

Hirsch records a case in an infant, aged 11 weeks, in whom the lethargy was not so marked as in older children, but the choreiform movements were pronounced. There was slight strabismus, but no other signs of ocular palsy were present. Recovery took place. Mouriquand and Lamy report an example of the myoclonic type in an infant aged five months which proved fatal at the end of the third week.

Pipping has observed lethargic encephalitis in five children whose ages ranged from 6 to 14 years. Two of these cases were comparatively benign, and in each the symptoms included headache, fever, restlessness, insomnia, succeeded by great drowsiness, and diplopia. In one case there was ptosis, with twitchings of the limbs lasting day and night. In the more serious cases there was a history of vomiting, violent headache and delirium with diplopia and hallucinations. In these cases, too, great drowsiness was preceded by insomnia. The ultimate fate of these three patients was still uncertain, and the aetiology of their disease was obscure. There was no history of influenza; these cases were perfectly sporadic, and in none had any other member of the family been similarly affected.

Lethargic encephalitis and epidemic hiccough. The relation between epidemic hiccough and lethargic encephalitis, to which attention has been previously drawn (vide *Medical Science,* 1920, **2,** 409; 1921, **3,** 481), has recently been discussed by Lhermitte, Rivet and Lipschitz, Netter (3), Lemoine, Dargein and Plazy, whose testimony confirms the truth of Lhermitte's striking phrase that 'epidemic hiccough is merely a fragment of the symptomatic mosaic of lethargic encephalitis'. Cases in which hiccough has preceded the development of lethargic encephalitis have been recorded by Rivet and Lipschitz, Sicard, Netter, and Dargein and Plazy, and examples of lethargic encephalitis having been transmitted by persons suffering from epidemic hiccough have been published by Netter (3), Lemierre, and Lemoine.

The close pathological relationship between the two conditions is shown by the account of an autopsy on a case of epidemic hiccough reported by Clerc, Foix, and Mercier des Rochettes. This patient was a woman aged 68, in whom the hiccough had lasted for six days. On the seventh day the temperature rose to 100·4, and the patient became somnolent. At the autopsy nothing remarkable was seen with the naked eye, but histological examination showed the lesions characteristic of epidemic encephalitis, namely perivascularitis, lymphocytic infiltration, and cellular changes. The lesions, however, instead of being situated in the brain and cerebral peduncles as in lethargic encephalitis, were practically confined to the cervical portion of the cord in which the centres of the phrenic nerve are located.

Kahn, Barbier, and Bertrand report a similar case of epidemic hiccough in a woman aged 52, which proved fatal in two days. At the autopsy the lesions in the central nervous system resembled those of epidemic encephalitis, but differed from them in their localization, being principally situated in the bulbar and cervical regions.

Sicard and Paraf record two cases of lethargic encephalitis complicated by spasmodic laughter and attacks of yawning respectively, which like hiccough they regard as due to disturbance of the respiratory function. A similar case of spasmodic laughter is reported by Netter in the discussion on their case.

The cerebrospinal fluid. Boveri, of Milan, who has examined the cerebrospinal fluid in 16 cases comes to the following conclusions: (1) The cerebrospinal fluid in lethargic encephalitis cannot be regarded as normal. (2) The changes in the fluid, however, are very moderate, both as regards the cellular content and the presence of albumin and reducing substances. (3) The cerebrospinal fluid shows the same scarcity of changes at all stages of the disease, but the changes are most easily demonstrated in the early stage. (4) There are no changes in the cerebrospinal fluid characteristic of any one type of epidemic encephalitis. (5) The slight character of the changes and their uniformity at all stages of the disease are two very important factors in the diagnosis of lethargic encephalitis from various forms of meningitis.

Findlay and Shiskin, who examined the cerebrospinal fluid in 23 cases in children, describe its characteristics as follows: clear scanty cellular contents, positive Fehling's test, excess of globulin, and especially the definite precipitation of the gold in Lange's test in the luetic zone with a negative Wassermann reaction.

As the result of the examination of the cerebrospinal fluid in 42 cases, Bonnard comes to the following conclusions: (1) In the great majority (89 per cent.) the cerebrospinal fluid shows a more or less marked lymphocytosis with or without an excess of albumin. (2) Excess of albumin with or without lymphocytosis is too inconstant (43 per cent.) to be taken into consideration. (3) Lymphocytosis associated with a normal or nearly normal amount of chlorides is of diagnostic value in distinguishing epidemic from tuberculous meningitis.

Moriez and Pradal, of Nice, also emphasize the importance of estimating the chlorides in the lumbar puncture fluid so as to eliminate at an early stage the diagnosis of tuberculous meningitis in which the amount of chlorides in the cerebrospinal fluid is always reduced, whereas in lethargic encephalitis it remains normal or high.

Foster, of the Massachusetts General Hospital, who reports the laboratory findings in the cerebrospinal fluid in 11 cases of epidemic encephalitis, found hyperglycorachia in all but one. There did not appear to be any definite relation between the duration of the disease and the excess of glucose in the cerebrospinal fluid, but it was found that the severest cases gave the highest sugar percentage and that during an exacerbation the percentage was likely to increase. There was no evidence of a corresponding glycaemia or glycosuria.

Davis and Kraus, of the Bellevue Hospital, New York, examined the cerebrospinal fluid of 35 cases of epidemic encephalitis, and in 14 or 41 per cent. found the type of colloidal gold reaction. This abnormality suggested syphilis, but there were no other serological or clinical evidences of this disease. The writers conclude that abnormal colloidal gold reactions are evidence of pathological changes and not of a specific aetiology.

Duhot and Crampon record six cases of epidemic encephalitis in which the Wassermann reaction was positive in the cerebrospinal fluid though negative in the blood. Syphilis could be excluded by the history and course of the disease and also by the reaction becoming negative in convalescence without specific treatment. Guillain's colloidal benzoin reaction was constantly negative in all the cases.

Diagnosis. Marie and Lévy describe the following points of difference between the Parkinsonian syndrome in lethargic encephalitis and typical paralysis agitans: (1) The age of onset is very different in paralysis agitans, which very rarely appears before 45 and generally does not develop till 50 or even over 60. The Parkinsonian syndrome, on the other hand, appears as a rule between 20 and 40, which is the period of life when lethargic encephalitis is not frequent, and may even occur in childhood. (2) The pre-existence of a general disease, usually febrile in character, occurs in the case of the Parkinsonian syndrome, whereas there is no such history in the case of paralysis agitans. (3) The mode of onset is very different in the two conditions. In paralysis agitans the onset is essentially progressive, being attended with a sensation of stiffness in one limb or segment of a limb or a slight tremor in one extremity. The condition appears to remain the same for some time or progresses only very slowly, and a few months later the other limb on the same side begins to show tremors. The onset of the symptoms in paralysis agitans therefore occurs in a progressively hemiplegic manner. In the Parkinsonian syndrome, on the other hand, a general stiffness develops in a few days, the face being apparently first affected. (4) The tremor of the hands typical of paralysis agitans is absent in lethargic encephalitis, although involuntary movements of the limbs or segments of the limbs, and even tremors of greater or less amplitude, are far from rare. (5) Difficulty in protruding the tongue and the presence of tremors in the tongue when protruded are frequent in encephalitis, whereas abnormal movements of the tongue are rare in typical paralysis agitans. (6) In encephalitis mastication occurs in an abnormal manner, being carried out almost exclusively with the incisors to the exclusion of the molars, and trismus is also frequent, whereas nothing of the kind is observed in lethargic encephalitis. (7) The evolution of the disease is distinctive. Whereas recovery from paralysis agitans is unknown, the writers have seen several mild cases in which the Parkinsonian syndrome has almost entirely disappeared.

Achard remarks that Sydenham's chorea is undoubtedly most frequent in early life, whereas epidemic encephalitis occurs later. Chorea is often preceded by articular rheumatism, chronic joint trouble is not uncommon, and heart disease is frequent. On the other hand, though pains in the joints occur in myoclonic encephalitis, true arthropathies and endocarditis are absent. The onset of chorea is usually gradual in contrast with the characteristic acute onset of encephalitis, and fever is usually absent. In chorea the movements are more extensive and complex, and are less limited to one muscle or groups of muscles. Sometimes, however, a distinction cannot be made, and Achard has no doubt that some cases described as chorea are really examples of encephalitis.

Souques also suggests that the ordinary chorea of children may in some cases be due to lethargic encephalitis, or in other words, form its sole clinical manifestation. Comby agrees with Souques in believing that there are grounds for dissociating Sydenham's chorea, the disease being polymorphous rather than uniform. There are considerable differences between the slight abortive cases and the intense hyperthermic attacks which may be described as acute or even hyperacute chorea. Comby does not hesitate to regard as instances of epidemic encephalitis the fatal cases of chorea, of which he has seen six examples among 560 personal cases of chorea.

Considerable difficulty in diagnosis is liable to arise when the myoclonic movements are localized in the pharyngeal or abdominal muscles. Denyer and Morley record a fatal case of myoclonic encephalitis simulating hydrophobia in a woman, aged 25, in whom death seemed to result from rupture of one of the constrictor muscles of the pharynx, due to extreme spasm causing subcutaneous emphysema with resulting cellulitis and aspiration pneumonia. Mauclaire reports a fatal case in a woman, aged 68, who presented symptoms of intestinal obstruction, and is of opinion that owing to the sudden and frequent contractions of the diaphragm and muscles of the abdominal wall a spasmodic intestinal obstruction took place, caused by trauma of certain parts of the intestine. Similar cases had been previously described by Massari (vide *Medical Science*, 1920, **2**, 409). On the other hand, Kummel and Fol report a case of intestinal obstruction with contraction of the diaphragm resembling the myoclonic form of lethargic encephalitis, but really caused by a fatal nephritis.

Merklen, who records a case of meningeal haemorrhage characterized by somnolence, torpor, and ptosis, remarks that lethargic torpor is not sufficient to justify the diagnosis of encephalitis, as one symptom does not constitute a disease. He objects to the term ‘lethargic encephalitis’, as the notion conveyed thereby tends to make the practitioner forget the forms of somnolence due to other marked processes. Rathery and Bonnard also report a case of meningeal haemorrhage simulating lethargic encephalitis.

Among other conditions recently described simulating lethargic encephalitis are general miliary tuberculosis with central involvement (Fiessinger and Janet), diffuse sarcomatosis (Fiessinger and Janet), hysterical narcolepsy

(Guillain and Lechelle (2)) veronal poisoning (Macleod), and suppurative ependymitis of the mesencephalon (Loeper and Forestier).

Prognosis. Cruchet, in collaboration with Moutier and Calmettes, has been able to trace 28 of the 40 cases of epidemic encephalomyelitis which he described in April 1917. 8 or 28·5 per cent. were dead. 6 or 21·4 per cent. were in a stationary condition, 2 of these being mental forms, 1 a bulbo-pontine, and 1 a spinal form. 8 or 28·5 per cent. showed slight improvement, 7 of these being hemiplegic forms and 1 a convulsive form. 4 or 14·2 per cent. showed an almost complete recovery, one of these being a mental form, 2 meningo-encephalic forms, and 1 a chronic form. 1 or 3·5 per cent. had a relapse.

In a subsequent paper Cruchet (3) records the outcome of 32 cases observed by him from March 1918 to February 1921. 13 of these belonged to the bulbo-pontine form, 8 to the meningo-encephalitic, 7 to the mental, 2 to the convulsive, and 1 each to the hemiplegic and spinal forms. 12 cases or 37·5 per cent. were fatal, and of the remaining 20 the great majority developed myoclonic symptoms resembling paralysis agitans or mental disorders. Cruchet concludes that though as regards life recovery is relatively frequent the occurrence of grave sequelae should warrant a guarded prognosis.

According to Hess of the Cologne University Medical Clinic, who has recently had the opportunity of examining 17 cases (13 men and 4 women) who contracted encephalitis in the epidemic of 1919–20, the prognosis of epidemic encephalitis is always serious as regards complete recovery. All his cases had numerous complaints, the principal being diminished power of work, loss of memory, and power of concentration, and a general lack of interest. Complaints of insomnia were very frequent. About 50 per cent. suffered from constant or occasional headache, which was sometimes so violent that work of any kind was impossible. Other complaints were neuralgia and rheumatoid pains, and diminution of sexual appetite both in men and women. All the patients agreed that their symptoms were aggravated by bad weather.

Prophylaxis. Netter (1) maintains that the patient should be isolated during convalescence as well as during the acute stage. He admits, however, that isolation cannot be made compulsory, as it is impossible to say when it should end, relapses being liable to occur after months or years. He also recommends disinfection of the patient's room, body linen, and clothes. Lastly, he is strongly in favour of making lethargic encephalitis a notifiable disease in France, as it has been in England since December 1918, in Italy and Switzerland since February 1920, in Portugal and Uruguay since June 1920, and in New York state since July 1920.

Treatment. Marie and Bouttier have found that subcutaneous injection of cicutine in non-toxic doses has a sedative action on myoclonic movements in epidemic encephalitis. If the symptoms are very marked they start with a small dose and give only ½ mgm. the first day to test the susceptibility of the patient. A daily dose is then given for four or five days and increased to 1–3 mgm. according to the state of the patient and the effect obtained. After five days the drug is usually suspended for two or three days, during which the urine, reflexes, and blood-pressure are examined. When the myoclonic symptoms become less intense but still persist, the injections are given only two or three times a week. The subsequent procedure depends upon whether there is a tendency to improvement, in which case the same doses are continued, or the reverse, when the dose is progressively increased if the drug is well tolerated.

Crofton and Costello, the former of whom had previously reported four cases in adults who rapidly improved after subcutaneous injection of pure influenza antigen (vide *Medical Science*, 1920, **2**, 413) record another case in which this treatment was equally successful.

The following methods have also been recommended: intragluteal injection of convalescents' serum (Grünewald), subcutaneous injection of convalescents' cerebrospinal fluid (Collatino and Vegni), intraspinal autoserum-therapy (Brill), subcutaneous autohaemotherapy (Bourges and Marcandier), and intramuscular injection of iodine oil (Muller).

Lhermitte classifies the methods of treatment of epidemic hiccough into two groups. The first comprises the drugs combating bulbo-spinal and vagophrenic hyperexcitability, such as belladonna, atropine, cocaine, morphia, bromides, camphor, and oxygen. The second group consists of physical methods used to inhibit the nerve centres which are in a state of reflex erethism, such as compression of the vertebral column (Nothnagel, Réthy), upper limbs (Piretti), ulnar nerve (Pauzot), eyeballs (Sicard and Paraf), and diaphragm by forced flexion of the lower limbs (Jödicke), or by an apparatus (Boyer, Rostan), distension of the oesophagus (Sicard and Paraf), and stomach (Kaimgiesser), ice-bag to epigastrium (Eloy), direct compression of the phrenics against the scalenes (Leioir, Grognot), faradization of the phrenics (Dumontpallier), and tongue traction (P. Lépine). Although these methods have only a relative efficacy, Lhermitte remarks that they are perfectly harmless.

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J. D. R.
C. L.

VINCENT'S DISEASE

Epidemiology. Attention was recently drawn (vide *Medical Science*, 1920, **2**, 545) to the unusual frequency in Germany of Vincent's disease, a term which includes not only Vincent's angina and stomatitis but also all other manifestations due to the symbiosis of the fusiform bacillus and spirillum, such as noma and phagedaenic ulceration of the genitals and neighbouring parts, as well as of other areas of the skin. The continued prevalence of this disease in Germany forms the subject of papers by numerous writers such as Sachs-Müke, Neste, Marx, Hage, Brüggemann, Plaut, Buschke, Meyer, Heck, Rahnenführer, Schwerin, and Gärtner. This prevalence is attributed by Sachs-Müke and Heck to under-nourishment. Heck emphasizes the predilection of Vincent's angina for patients suffering from leukaemia and other exhausting diseases, and alludes to scurvy, a clinically allied disorder, being undoubtedly the result of nutritional disturbance. He finds further support for his view in the general decline of personal cleanliness due to lack of soap and heating material, which has led to an increase of skin disease and is possibly responsible for lesions of the mucous membranes.

On the other hand, under-nourishment as an explanation of the prevalence of Vincent's disease is denied by other writers, such as Reiche, Neste, Brüggemann, Hage, Rosenberger, Rahnenführer, and Gärtner, who note its predilection for vigorous young persons of both sexes, and also point out that it did not become prevalent until 1919, when the supply of food was much more plentiful and richer in vitamins than during the last years of the war. Rahnenführer states that the disease is particularly frequent in the East, especially in the Balkans, as was recently illustrated by David and Hecquet (vide *Medical Science*, 1920, **2**, 546), and suggests that the present dissemination of the disease is connected with the return of soldiers from those parts, while Rosenberger considers that it is the coloured troops of the allies that brought the contagion to Europe.

Gärtner, however, is sceptical as to the likelihood of Vincent's angina having been introduced into Germany by troops returning from the Balkans. He states that he never met with a single case while he was in Turkey, where the number and clinical character of gingivitis cases did not differ from those seen at home. He points out that the prevalence of the disease among the Balkan troops has not been proved, and at the time of demobilization the comparatively few soldiers left in the Balkans were elderly and insusceptible men belonging to the Landsturm or Landwehr, who were not likely to have infected the younger members of the civilian population on their return home.

In a study of Vincent's angina at a base hospital at Camp Devens, Massachusetts, from April 1918 to July 1919, Reckford and Baker found that the number of cases began to increase in August, rose slowly to September, remaining stationary to December, with a rapid rise in February and a decline below that observed in the previous September. In their series of 56 cases 52 were white and four black. The average age was 24½ years. In only 8 cases was there a history of exposure to infection.

Gärtner, assistant at the Kiel University Institute of Hygiene, emphasizes the difference in the age and sex distribution of Vincent's angina and diphtheria respectively. Vincent's angina is most frequent between the ages of 16 and 30 years, a few cases occurring before and a few after that period. Of 294 cases about whom information was obtained at Kiel 188 were males and 106 females, so that the disease was 50 per cent. more frequent in the male sex. Diphtheria, on the other hand, showed a preference for the female sex. Of 2,226 cases at Kiel 1,275 were females and 951 males. Although up to the age of 7 years boys were more frequently attacked, between 9 and 13 the disease was commoner in girls. After school age its frequency diminished in both sexes, but in a less marked degree in the female sex. After the eighteenth year the greater prevalence of the diphtheria among women was undoubtedly due to their greater frequency of exposure to infection in their capacity as nurses, teachers, or mothers.

Symptomatology. Reiche, who has seen 193 cases of Vincent's angina or stomatitis at the Hamburg-Barmbeck Hospital since 1904, confirms the prevalent view as to the usual harmlessness of the affection. Even when the lesions are almost exclusively confined to the larynx, of which only a few examples have been recorded (vide *Medical Science*, 1920, **2**, 546–7), the benign character of the attack compared with laryngeal diphtheria is striking. In a few instances, however, Reiche met with some severe and even fatal complications, including renal disease, myocardial changes, and peripheral palsies. (Probably in those cases a coexistent diphtheria had been overlooked.—J. D. R.). In a case of extensive old mesenteric tuberculosis in a girl, aged 4 years, an attack of Vincent's angina hastened a fatal termination.

Rahnenführer records a fatal case in a boy aged 12 years, in which Vincent's angina was complicated by gas-gangrene septicaemia due to Fraenkel's gas-gangrene bacillus.

Souchet records a case illustrating the difficulties of diagnosis when a tonsillar chancre is complicated by fuso-spirillar infection. The clinical and bacteriological appearances of his case were those of Vincent's angina, and it was not until the appearance of a cutaneous eruption that the presence of syphilis was suspected, when the *Spirochaeta pallida* was found in addition to Vincent's organisms, and a positive Wassermann reaction was obtained. Souchet emphasises the dangers of a hasty and incomplete bacteriological examination in cases of persistent ulcero-membranous angina, and states that in doubtful cases one should not be content with a superficial scraping of the diphtheroid deposit, but should examine the serum oozing from the ulcer, as in this way the *Spirochaeta pallida* may be found in addition to Vincent's organisms.

The coexistence of diphtheria to which Rolleston (1) and others have previously drawn attention is emphasized by Meyer, who states that Vincent's angina may occasionally mask diphtheria, the existence of which is proved by the failure of the ordinary treatment for fuso-spirillar infection and the subsequent development of characteristic paralysis.

Hennessy and Fletcher of Kuala Lumpar, Federated Malay States, report a case of infection with Vincent's organisms following man-bite. The left thumb, which was bitten, was swollen and indurated. The nail was replaced by a soft mass of granulation tissue with sinuses leading down to the fractured phalanx, and at the base of the thumb was an abscess which involved the metacarpo-phalangeal joint, the pus from the sinuses containing fusiform bacilli and enormous masses of spirochaetes. The extent of the disease and severity of the pain rendered amputation imperative. Recovery took place.

Koslowsky reports a case of auto-inoculation of the skin of the anal region with Vincent's organisms in a boy aged 10 years suffering from Vincent's angina.

Several British otologists, such as Cheatle, Adam, and Wingrave and Ryland, have recently described infection of the external auditory meatus and middle ear with Vincent's organisms. In Cheatle's two cases, in which the process was confined to the external auditory meatus without involvement of the middle ear, the meatal infection was probably secondary to a gum infection and had been conveyed by the fingers to the ear. Adam, who has observed 30 cases of Vincent's infection of the external auditory meatus and middle ear, all but one of which were in children, has always found the condition to be associated with neglect, and to be a graft upon a previous pyogenic infection of the middle ear, as evidenced by the history of the case, appearance of the patient, and carelessness as to treatment. The meatus is lined with granulations interspersed with shreds of greyish membrane. Marked tenderness of the meatus and foetor are characteristic features of the condition.

A fatal case in a child of gangrenous perichondritis of the ear and otitis media from invasion of fuso-spirillar infection from the throat is reported by De Rezende. Almost the entire ear and the neighbouring parts sloughed off down to the posterior wall of the tympanic cavity. The other ear also showed commencing otitis media. Under local treatment with a neutral solution of chlorinated soda and Peruvian balsam the process was arrested and healed, but the child succumbed later to cachexia and auto-intoxication.

Donovan, of the University of Wisconsin Medical School, records a case of what is sometimes known as the fourth venereal disease or ulcerative and gangrenous balano-posthitis due to infection with Vincent's organisms, of which only two examples have been published in the United States, by Ross and Bond respectively (vide *Medical Science,* 1920, **2**, 547), since Corbus and Harris drew attention to it in 1909.

Mouriquand, Gaté, and Hughes examined the Wassermann reaction in sixteen cases of Vincent's angina which had persisted for several weeks and was associated with severe constitutional disturbance and a temperature ranging from 100·4 to 101·2, and found the reaction persistently negative. They have also collected sixty cases from the literature of the last ten years which all agree in showing that the fuso-spirillar association is incapable by itself of producing a positive Wassermann reaction. They therefore conclude that the presence of a positive Wassermann reaction in Vincent's angina should always indicate syphilis. In 1912, however, Rolleston (2) published a case of severe Vincent's angina in a girl aged 5 years without any family history or personal evidence of syphilis, in whom the Wassermann reaction was positive at first but became negative a fortnight later without antisyphilitic treatment. He also alluded to similar cases of a positive Wassermann reaction in Vincent's angina apart from concomitant syphilis, which had been reported by Gerber, Much, and Saverio.

Treatment. Local treatment of Vincent's angina by *salvarsan* is often effectual in obstinate cases, as has been shown by Rolleston (3) and others. Local application of a concentrated watery solution of *neosalvarsan* is recommended by Brüggemann. Hirsch, of Stuttgart, however, has found that several cases proved refractory to local treatment by salvarsan but cleared up after one, two, or at most four intravenous injections of 0·45 to 0·75 gm. neosalvarsan. Borrello, of the Palermo Institute of Clinical Paediatrics, who records six cases in children aged from 3 to 7 years, also regards intravenous injection of neosalvarsan as the most efficacious method of treatment both in respect to its rapidity of action and its absolute innocuity. *Silver-salvarsan* in doses of 0·05 to 0·1 gm. has likewise been found of value by Hirsch.

During the last year Rahnenführer has found that *trypaflavin* acts almost as a specific on Vincent's angina or stomatitis, though it has no special action on diphtheria or follicular tonsillitis. It is used in the form of a ½ per cent. spray to the affected tonsil two or three times a day. Twenty drops of a ½ per cent. solution to a glass of water are also used as a gargle. The deposit on the tonsil or gum disappears in five or six days on the average with this treatment, whereas local application of salvarsan does not act so rapidly. Trypaflavin also has the advantage of being cheaper than salvarsan.

Bennigson has adopted Barth's method (vide *Medical Science*, 1920, **2**, 548) of applying a 10 per cent. solution of *salicylic acid* in equal parts of alcohol and glycerine in cases which had been treated for weeks unsuccessfully by tincture of iodine, chromic acid, and silver nitrate. He considers this treatment better than the use of neosalvarsan, as cases of syphilis so treated may be mistaken for Vincent's angina and thereby run a risk of receiving inadequate treatment subsequently.

Marx has obtained excellent results in the treatment of Vincent's angina by the use of *pyoktanin*, a 1 per cent. solution of which is applied to the affected part until it is of an intense blue colour. The patient is also given a two-hourly gargle of chlorate of potash.

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J. D. R.

THE NERVOUS CONTROL OF MICTURITION

Micturition is the process by which the bladder normally empties itself. In the intervals between separate acts of micturition urine is retained in the bladder by the tonic contraction of the plain muscle surrounding the posterior urethra and of the compressor urethrae. Though the contraction of the compressor urethrae is stronger than that of the plain muscle of the posterior urethra (Courtade and Guyon) urine is held at the internal urethral meatus (Griffiths, Rehfisch) so that the posterior urethra is closed until micturition commences. In man the posterior urethra, at any rate down to the verumontanum, can be removed without causing incontinence of urine, as is shown by the fact that this disability does not follow suprapubic enucleation of the prostate; in such cases urine is held by the compressor urethrae (Walker). In micturition there is a sustained contraction of the bladder and a simultaneous relaxation of the closing mechanism of the urethra. Both these are evident from observations on man, the first from the fact that the force of the stream is maintained nearly to the end of the act, and the second from the well-known clinical observation that a posterior urethral irrigation can be performed with a lower pressure if the patient tries to micturate voluntarily than if he does not.

The bladder derives its nerves from the hypogastric plexus. The hypogastric plexus is formed by branches of two pairs of nerves, the pelvic nerves arising from the sacral plexus and the hypogastric nerves arising from the inferior mesenteric ganglia, which in their turn are connected centrally by the lumbar splanchnic nerves with the lumbar ventral roots (Budge (1), Gianuzzi). In addition to the pelvic and hypogastric nerves the urethra receives branches from the pudic nerves, and from gross dissection it can be seen that the compressor urethrae is supplied from branches of these nerves. All three pairs of nerves are known to contain afferent as well as efferent fibres, but as their distribution is not exclusively to the bladder and urethra it does not follow from this fact that the afferent fibres in any particular case are those of the bladder or urethra. The particular nerve-roots which give fibres to the bladder vary in different species of mammal and to a slight extent in different individuals of the same species (Langley and Anderson, Sherrington), but in all species investigated the lumbar and sacral roots concerned are separated by intervening roots which contain no bladder fibres. Like other visceral nerves the bladder fibres of both the sacral and lumbar roots are interrupted by ganglion cells; in the case of the sacral roots these are situated peripherally in the hypogastric plexus, but for the greater part of the lumbar fibres the relay takes place in the inferior mesenteric ganglia (Elliott, Langley and Anderson).

The action of the efferent nerves to the bladder and urethra. Stimulation of the peripheral cut end of one pelvic nerve causes a powerful contraction of the bladder chiefly on the corresponding side (Gianuzzi, Langley and Anderson); this result is obtained in all mammals on which the experiment has been made. Stimulation of the peripheral cut ends of both hypogastric nerves also causes contraction of the bladder, but this is weaker than that produced by stimulation of the pelvic nerves (Gianuzzi). The contraction produced by the hypogastric nerves in some animals, e. g.

the ferret, involves the whole bladder, but in others, e. g. the rabbit, is limited to the muscle between the ureters on its dorsal side (Elliott). Relaxation of the bladder follows the initial contraction and exceeds it in the cat and monkey (Stewart, Elliott), but in no other animals have inhibitor fibres to the bladder been certainly demonstrated in the hypogastric nerves by direct stimulation. Evidence of the existence of inhibitor fibres in other animals exists from the effect of adrenalin on the bladder after the administration of ergotoxin (Elliott).

Stimulation of the peripheral cut ends of the pudic nerves leads to contraction of the urethra and a similar result follows in the case of the hypogastric nerves (v. Ziessl). Peripheral stimulation of the pelvic nerves in both the dog and cat leads to relaxation of the urethra (Elliott, v. Ziessl).

The functional results of division of the peripheral nerves. (1) Both pudic nerves. This lesion in cats constantly produces some degree of incontinence which varies between the escape of a few drops only, when the bladder is gently squeezed from the outside, to the dripping away of urine when the cat is quietly walking about. The condition remains unaltered at any rate for weeks, and it is not made worse by dividing both hypogastric nerves (Barrington).

(2) Both hypogastric nerves. Micturition takes place quite normally after this lesion (Mosso and Pellacani). Incontinence of urine does not occur and urine is still held at the internal meatus and not at the compressor urethra (Barrington), showing that the contraction of the so-called internal sphincter of the bladder is not due to a nervous tone. Division of both hypogastric nerves in cats does seem to produce a certain amount of frequency of micturition (Barrington).

(3) Pelvic nerves. Division of one pelvic nerve produces no appreciable effect on micturition, but division of both nerves in dogs and cats produces retention of urine, the bladder becomes greatly distended and submucous ecchymoses, haematuria, and ulceration may occur (Lannegrace). For some days the urine constantly drips away unless some means of emptying the bladder are adopted, but during this time the animal does not show the slightest sign of distress, indicating that the efferent impulses leading to urgency of micturition must pass to the central nervous system in the pelvic nerves. This condition lasts a variable number of days; after this time, in cats, the urine ceases to run away continuously, and therefore the animals remain dry; they carefully select spots which they consider suitable to pass urine on and squat down in the characteristic way and pass it, showing that they have a definite desire to micturate. When urine is passed, however, it is only in very small quantities and in a very feeble stream, and a large amount of residual urine is left in the bladder when they have finished (Barrington). When this stage is reached division of both hypogastric nerves has no effect on it, so that it cannot be due to the paralysis of the bladder wall having been compensated by a central nervous effect through these nerves. Division of both pudic nerves, however, abolishes this condition; urine then constantly drips away, so that the animal is always wet; it ceases to make attempts to pass urine, residual urine is always present, but in a smaller quantity than before the division of the pudics. Both the sensation of a desire to pass urine and the ability to do so, to some extent at will, in cats that have had the pelvic nerves divided, are therefore sometimes dependent on the pudic nerves. However, the sensation can only be a very insignificant part of the normal desire to micturate, since it takes

the cat days to learn what it means, while the ability to pass urine cannot depend on contraction of the bladder, since the pudic nerve does not supply the bladder, and must therefore be due to relaxation of the closing mechanism of the urethra only. It may be observed that, as far as micturition is concerned, division of both pelvic and both pudic nerves is the same lesion as destruction of the sacral region of the cord, since these are the only nerves concerned which arise from this part of the cord; the effects are therefore the same as those observed in destruction of the sacral cord (Goltz (1)).

(4) Division of the sacral dorsal roots. In dogs and cats (Merzbacher, Barrington) this lesion produces retention of urine, great distension of the bladder, and dripping away of urine. The animals show no signs of distress and do not attempt to micturate, the sphincter remains tightly contracted, and the condition is permanent.

Reflex micturition. If the bladder of an intact animal is gradually artificially distended with a warm inactive liquid, sooner or later it reacts with a powerful contraction expelling the liquid. This reflex is very markedly depressed by chloroform or ether. As will be described subsequently, normal acts of micturition take place in decerebrate cats, i. e. cats in which the mid-brain has been cut through just in front of the tentorium, and the brain in front of the section removed. Decerebrate cats therefore offer a means of investigating reflex micturition without the disturbing effect of anaesthetics or emotions. The bladder of a cat can be divided at its neck without disturbing the branches of the hypogastric plexus to any appreciable extent; if, when this has been done, a cannula is tied into each cut end the pressure of urethral resistance and the intravesical pressure can be observed simultaneously under varying conditions. In this way reflex micturition can be shown to consist of five reflexes (Barrington (3)).

(1) Distension of the bladder leads to a powerful, sustained contraction of the bladder. Both afferent and efferent paths of this reflex are in the pelvic nerves. This reflex is abolished by dividing the spinal cord or the brain anywhere behind the middle of the pons: it is also abolished by cocainizing the interior of the bladder (Shattock).

(2) Running liquid through the urethra leads to a powerful, sustained contraction of the bladder. The efferent path of this reflex is in the pelvic nerves, the afferent usually in the pudic nerves, but apparently in some cases also in the hypogastric nerves. Like the first, this reflex is destroyed by transection of the spinal cord or of the brain behind the middle of the pons.

(3) Distension of the posterior urethra leads to feeble, transitory contractions of the bladder. Both paths of this reflex are in the hypogastric nerves. The reflex is not destroyed by division of the spinal cord in the posterior thoracic region.

(4) Running liquid through the urethra leads to relaxation of the urethra. Both paths of this reflex as it was observed were in the pudic nerves; since, however, the muscle supplied by these nerves is much more powerful than the smooth muscle, the method of observation does not exclude the possibility of the other two pairs of nerves taking part in the efferent side of the reflex. The reflex is not destroyed by division of the spinal cord in the lower thoracic region, but is modified by this lesion; the modification is probably due to the abolition of a reinforcement of the reflex through the second and fifth reflexes.

(5) Contraction of the bladder provoked by distending it leads to relaxation of the urethra. The afferent path of this reflex is in the pelvic

nerves, and the efferent in the pudic nerves. The reflex is abolished by cocainizing the interior of the bladder, but not by dividing the cord in the posterior thoracic region.

The precise use of the third of these reflexes is not evident, but the other four are such that if one is evoked it brings the others into action in such a way that the effect of one is reinforced by another. The existence of these reflexes affords an explanation for the fact that urine is held at the internal meatus in intact animals, and at the compressor urethrae after lesions which destroy the first reflex (division of both pelvic nerves, of the sacral dorsal roots, or of the spinal cord), since the pressure necessary to force the internal meatus is greater than that which produces a reactionary contraction of the bladder.

The influence of the brain on the bladder. Stimulation of various parts of the mid- and hind-brain have been found to result in contraction of the bladder (Budge (2), Karplus, and Kreidl, Sokownin). This is not due to a general vasomotor effect, since it occurs after ligature of the abdominal aorta (Sokownin). The impulse travels down the cord and out through the sacral nerves, since it is abolished by division of the cord or of the sacral roots (Budge (2)). Stimulation of the cord leads to contraction of the bladder, which is very much diminished by division of the sacral roots, and completely abolished if the hypogastric nerves are subsequently divided (Sokownin).

Conversely, if, in a cat whose bladder is reacting with contractions to a slight increase in intravesical pressure, both pelvic nerves are divided, the contractions cease, and the bladder passively dilates and remains distended. The same effect is obtained if the central nervous system is divided at any level between the sacral region of the cord and the middle of the pons, but not if it is divided in front of this level (Barrington (3)). These effects are observed whether the hypogastric nerves are intact or divided at the time the lesion is made, and division of the hypogastric nerves after the lesion is not followed by a further dilatation, but, at any rate in lesions up to the mid-thoracic region of the cord, by a persistent contraction (Barrington).

The functional results of central nervous lesions. In the bitch from which Goltz (2) removed both cerebral hemispheres micturition not only appeared normal but the bitch squatted down in the position peculiar to intact bitches during micturition.

As already stated, decerebrate cats micturate normally; the stream has the usual force, it finishes with a few jets which can be seen to be due to perineal contractions, and the bladder is empty at the end of the act; being in decerebrate rigidity, the cat remains lying on its side during the act. Micturition seems to take place rather more frequently in decerebrate than in intact cats.

Transection of the spinal cord affects micturition in the same way, whatever the level, provided it is in front of the nuclei of the sacral nerve-roots, so that the pudic nerves are not interferred with. With such a lesion there is a period of retention of urine, and the bladder becomes distended and overflows as after division of the pelvic nerves. After a variable number of days the retention is succeeded by what is called spontaneous micturition. In this stage, which persists for the remainder of the animal's life, urine is only passed at intervals, and then in a series of forcible jets, the first in the series usually being the largest; in this way very considerable quantities of urine may be passed at a time. The passage of urine in jets at this stage can be easily provoked by cutaneous stimuli, especially in the perineal region, or by slight abdominal pressure squeezing a small quantity of urine into the urethra; if the cord behind the transection is destroyed, spontaneous micturition is abolished, and the bladder again continuously overflows(Goltz (1)). Spontaneous micturition is therefore certainly due to a reflex in the part of the cord behind the transection. Since the intravesical pressure is considerable it might be due to relaxation of the closing mechanism of the urethra, to contraction of the bladder, or, as in normal micturition, to both together. The last possibility is excluded by the fact that, at any rate in cats, a considerable and usually large amount of urine remains in the bladder at the end of the escape of urine. During spontaneous micturation the jets can actually be seen to synchronize with the relaxations between clonic contractions of the perineal muscles. If a cat in which spontaneous micturition has developed subsequent to a spinal transection is decerebrated, and the urethral resistance and bladder-pressure observed simultaneously by the method already described, the first and second reflexes described are found to be absent, and the remaining three present as immediately after the transection (Barrington (3)). Spontaneous micturition therefore is not due to any recovery of the central nervous control of the bladder improving its motility, but to relaxation of the closing mechanism of the urethra.

The term 'centre' has intentionally not been employed in this review as having previously been used in absolutely different senses, it would have led to ambiguity. If used as synonymous with an anatomical nucleus or as simply an expression of an experimental fact that artificial stimulation of a circumscribed region produces some effect more readily than the same stimulation elsewhere, it is correct to speak of a bladder centre in the sacral part of the cord. The term when applied to a function is, however, often used to indicate that the function can take place when the centre is completely separated from all other parts of the central nervous system. Used in this sense, the statement that a micturition centre exists in the lumbosacral cord is false in the case of the cat and devoid of proof, or even of probability, in the case of other mammals on which the experiment of spinal transection has been performed.

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F. J. F. B.

ABSTRACTS

SURGERY

BRAUS, H. *Anatomie des Menschen: ein Lehrbuch für Studierende und Ärzte.* Bd. I. *Bewegungsapparat.* [**'Human anatomy: a text-book for students and doctors'. Vol. I. Organs of movement.**] Berlin, J. Springer, 1921, pp. 835.

In this first volume of a new text-book of anatomy the author has broken away from many of the old conventions, and produced a work that is both more scientific and practical than the stereotyped books on anatomy. He never forgets that the chief object in studying the corpse is to understand the living body, and the book is freely illustrated with pictures of living models and fuller and more intelligent descriptions of how muscles and joints work than are usually found in students' books. The majority of the illustrations in the book are new and original in the sense that they present the essential facts of anatomy in a novel and impressive way. At a time when British publishers are warning authors to be sparing in the use of colours and half-tone illustrations, it is interesting to find that a German publisher can provide such a wealth of artistic half-tone drawings with so lavish—perhaps too lavish—a use of colours.

The author not only gives the student a very lucid account of the practical working of the human body and the underlying biological principles, but he also introduces in a skilful way a good deal of information about anomalies and features of anthropological significance. A noteworthy feature is the care and thoroughness with which the muscles of expression are described and their actions explained.

The publication of this book marks a welcome reform in the mode of presentation, but the German student must have greater enthusiasm and powers of assimilation than the majority of British students if he really reads a work of this size. G. E.-S.

FREDET, P. Sur quelques points de technique à propos de la résection du genou pour tumeurs blanches. [**Some technical points in resection of the knee for tuberculosis.**] *Bull. et mém. Soc. de chir. de Par.*, 1921, **47,** 1001–6.

Fredet points out that many of the classical methods of resection of the knee infringe very markedly the ideal rule that the operation should remove all of the tuberculous lesion without infecting healthy tissues. Certain surgeons have, in their enthusiastic desire to obey this rule, resected *en bloc* the whole knee-joint, including the femur and tibia to the full extents of their relationship to the joint; but by this operation so much bony length of the limb is sacrificed that the leg ceases to be of much use to the patient; it may therefore be condemned.

Fredet takes a middle course in that by his technique he removes the soft parts of the joint wholly, yet saws the bones at levels that allow the preservation of a limb of reasonable length. He does the major portion of the operation with the infected knee-joint unopened, and reserves the period during which it must be open, with possibility of implantation of the disease on healthy surroundings, to a late stage of the excision. He is enabled to do this by ceasing to regard the periosteum, lateral ligaments, &c., as possessing the importance attributed to them by the older surgeons.

Another interesting feature of his operation, which he has performed on thirteen patients, is that he saws the bones with the leg extended on the table, using two saws, one for the femur and the other for the tibia; the femoral one he leaves in position in his saw-cut just before completing the division, and then uses it as a guide whilst, with the other saw inserted parallel to the first one, he divides the tibia. The popliteal vessels are in the meantime guarded from injury by a metallic H-shaped retractor placed in front of them and behind the bones; the H-shape enables the retractor to lie flat and firmly during the sawing of the bones. The use of two parallel saws, with leg extended, saves him the trouble of judging the exact axes in which the saw-cuts must be made, for even if he should have cut one bone obliquely (an advantage when the distribution of the tubercle in the bone is higher at one side than the other) yet the parallelism of the cuts brings the leg into natural direction when the bone-ends are approximated.

His method is as follows: Good tourniquet haemostasis is obtained and a large U-shaped flap is made. The lateral limbs of the U must be placed as far back on the lateral aspects of the limb as possible; the apex of the U reaches the anterior tubercle of the tibia.

The lower part of the joint is then attacked; the synovial cul-de-sac and all soft tissues are dissected up from the lateral tuberosities of the tibia; the ligamentum patellae is divided near the patella, without opening the joint, and turned downwards. Then here, too, the soft parts and the synovial cul-de-sac are dissected up from the bone to the neighbourhood of the articular surfaces.

The quadriceps is divided above the patella, and the incision carried transversely outwards and inwards through the lateral parts of the muscle and aponeurosis until it reaches the supracondylar lines as far back as possible, near the bases of the supracondylar triangles. The quadriceps is then raised, so as to leave the fibrous capsule attached to the patella and synovial membrane; at this stage Fredet splits the quadriceps tendon longitudinally in line with the axis of the ligamentum patellae; in the later steps this facilitates the fixation of the tibia to femur in a line correct to secure the natural degree of rotation of the limb. The subcrureus is divided transversely above the synovial reflection, and, by cuts made close to the bone, the synovial sac is dissected down to the edge of the articular cartilage.

The lateral aspects of the condyles are denuded in the same manner; and the lateral ligaments and tendon of the popliteus are separated from their bony attachments.

Now for the first time the joint cavity is opened in order to permit separation of the posterior parts of the synovial membrane. The leg is strongly flexed on the thigh, the crucial ligaments are detached from their femoral insertions; the tibia and femur can now be separated from each other; the femoral extremity is protruded and the retro-condylar pouches dissected downwards, from outside, without danger to the popliteal vessels.

Similarly the synovial reflection is dissected up from behind the tibia and the bursa under the popliteus muscle removed with scissors. The end of the femur is now bare; the capsulo-synovial sac remains attached to the plateau of the tibia; by separating the menisci and the crucial ligaments from their tibial insertions, the mass is then rapidly removed in one piece by following all its diverticula and contours from without. The leg remains attached to the thigh merely by the posterior band of tissues containing popliteal vessels and nerve. The bones having been examined are sawn across in the manner described above, after placing the H-shaped retractor between them and the popliteal fasciculus of tissues.

The tourniquet is removed, haemostasis secured, and the bone-ends fastened to one another by the use of wires.

To avoid faulty rotation of tibia on femur it is only necessary to see that the split made in the quadriceps is placed in line with the axis of the ligamentum patellae.

Note: The method seems to have much to recommend it, especially the lateness of opening into definitely diseased tissue, the complete extirpation from without of the synovial sac, the ingenious parallel saw method of dividing the bones to secure correct axis of the limb, and the marking of the quadriceps to avoid fixing the bones unduly rotated on each other.

C. C. C.

Vignard, P., et **Vincent, E.** Ankyloses du genou d'origine tuberculeuse chez l'enfant, leur correction. [**Ankyloses of the knee of tuberculous origin in children, and their correction.**] *Rev. de Chir.*, 1921, **59**, 7.

The authors give a brief historical review of the progress of the attitude of surgery towards ankylosis, pointing out that its aims are firstly to prevent, and secondly to treat this condition. They then discuss the pathology of osteoarthritic tuberculosis, and describe how it may lead to a movable joint, but more commonly results in a fibrous or bony ankylosis.

They emphasize, with reference to a number of authorities:

(1) That immobilization alone can never produce bony ankylosis.

(2) That immobilization can produce only a false ankylosis by contractures of muscles.

(3) That immobilization can produce eventually a movable joint if the disease for which it be applied be insufficient to destroy the articular surfaces and the peri-arthrodial structures; and that therefore it is the only correct treatment for slight cases of joint tuberculosis.

(4) Conversely, that mobilization of a joint neither prevents nor delays ankylosis if the condition of the joint be such as to entail it, but may even be the cause of its occurrence by favouring the development of ulceration and consequent adherence of the articular cartilages.

(5) Further, that movement of a tuberculous joint not only aggravates the lesions of the cartilages, but tends to favour the eventual occurrence of ankylosis in flexion. A tuberculous or otherwise infected knee, if left alone, never becomes ankylosed in extension; as the muscles around the joint atrophy, the more powerful flexors in the absence of treatment always cause flexion. As a result of this position of flexion, the articular surfaces become modified by bony rarefaction at the points of pressure. This results in the erosion of the condyles of the femur posteriorly, and the overgrowth of their anterior parts in a forward and downward direction,

possibly as a result of irritation by the disease of the epiphyseal cartilages; therefore the backward displacement of the tibia and the deformity of its upper extremity which sometimes occurs. Flexion deformity can equally result from an intra- or extra-epiphyseal resection of the knee, where the after-treatment is inadequate. Further, if a resection be performed, the patella may be removed, a proceeding which throws the quadriceps out of action and removes opposition to the natural tendency to the production of flexion. The authors consider, in opposition to the theories of Broca, that the cartilaginous deformities are the result rather than the cause of the onset of flexion.

In examining an ankylosed joint the three things to consider are: Is the ankylosis fibrous or bony? Is the tuberculous process healed? and, what is the condition of the muscles acting on the joint? The last is of little importance unless the surgeon is considering the production of a movable joint.

The treatment. (*a*) It should be prophylactic. In slight cases rigorous immobilization favours the return of movements by early healing of the tuberculosis. Immobilization of the knee in an adult should be at an angle of 15 degrees, so as to avoid undue movement of the pelvis in walking. In a child the shortening resulting from the disease makes an ankylosis in complete extension preferable. In a child also the immobilization should be carried on until the end of the period of growth. If ankylosis has occurred in malposition, the authors do not consider that correction should be delayed until the period of growth is complete, but think that, if the tuberculous process has completely healed, correction of faulty position of the knee will prevent the development of static deformities in the pelvis and vertebral column.

(*b*) Should treatment attempt to cure ankylosis? The various operations of arthroplasty of the knee are reviewed, as also those where grafts of articular cartilages or whole knee-joints are employed. All are condemned as unsuitable for children anyhow, being unlikely to produce a good mobile joint and likely to produce an unstable one. The surgeon should therefore either prevent the occurrence of ankylosis or he should respect an ankylosed joint, being content to correct any deviation from the axis of the limb, while preserving the solidity. Correction may be bloodless or by open operation. The authors then review the various forms of osteotomy, linear and cuneiform. For any deformity of the knee to an angle of less than 90 degrees, simple supracondylar osteotomy is contra-indicated, as the resulting correction involves a considerable backward deformity of the lower fragment of the femur. A double osteotomy has been done, but this is difficult. Cuneiform osteotomy with resection of part of the condyles is contra-indicated in children because of its interference with growth. Transarticular operations have the disadvantage that they are liable to stir up the tuberculous process. Resections are indicated only in children who have completed the growing period. However, in severe deformity, as in the case of Tavernier (*Revue d'orthopédie*, 1919), where the leg was parallel to the thigh, resection may be the only possible operation.

Bloodless operations: Supracondylar osteoclasis, originally produced in attempts at forcible rectification at the level of the joint, has been made a precise procedure by the ingenuity of Robin and Ollier, who used Robin's osteoclast. First designed for the correction of genu valgum, this instrument enables the operator to break the bone exactly at the level desired.

Details of the method of using the osteoclast are given. The fracture should be made at the lowest possible point, and the application of force should cease at the first crack, which may be so slight as to be audible only to the operator; a complete fracture should not be made. The limb is then put in a plaster case in its deformed position and reduction of the deformity is made by successive stages beginning five to six days after the osteoclasis. This permits of gradual stretching of the contracting structures of the popliteal space.

Objections raised to the procedure are: (1) That it is a blind method. They answer that following closely Robin's method in 2,000 cases it was precise. (2) That there is danger to vessels and nerves. But damage to these structures has not occurred in the author's experience; there are no loose fragments of bone, such as are seen and such as have caused serious wounds of the femoral artery in the performance of osteotomy. (3) That it gives a frail union. That this is not so has been shown *post mortem*. The fracture after osteoclasis is consolidated in less than thirty days as a rule. (4) That it is theatrical. Though the force employed is often more than 100 kgm. the instrument enables the fracture to be made with invariable gentleness, and the procedure is no more brutal than the reduction of a dislocated shoulder by Kocher's method. (5) That it results in a Z-shaped deformity. This fault is due to using the method in cases where the deformity is great, and the same objection applies to osteotomy. In cases where the angulation is great, recourse should be had to arthroclasis. This aims at producing a fracture at the apex of the curvature, and is specially suitable for children. The instrument used is a modification of the osteoclast. It is especially suitable for those cases where there is displacement of the tibia. If there is bony ankylosis it has been a matter of doubt whether the opening up of the back of the joint and the creation of a space between the bones would be followed by the filling up of this space by new bone. In children and adolescents epiphyses are capable of producing union. Arthroclasis then has advantages over all other procedures inasmuch as it is free from danger; and by correcting the deformity at the summit of the curvature it does not add to the shortening, due to the disease, a further shortening due to treatment.

If performed not less than three years after the tuberculous process has healed there is no danger of stirring up the disease, and this applies to all forms of correction of deformity. Neither general nor local tuberculosis has been aroused by the procedure. After correction it is important that a splint should be worn until the period of growth is over.

Eight cases, where arthroclasis has been employed, are quoted and radiograms shown in patients whose ages ranged from 8 to 15 years.

The authors sum up by saying that: (1) restoration of mobility in the knee is not a satisfactory proceeding; (2) treatment should be confined to correcting deformity; (3) in obtuse agglutination of the knee, supracondylar osteoclasis is indicated.

Where the angulation is less than 130–140 degrees, extra-articular correction is contra-indicated because it increases shortening due to disease by that due to the situation due to the correction. In these cases arthroclasis should be used which corrects at the apex of the curvature. If necessary, simultaneous osteoclasis of the tibia may be employed. Arthroclasis is indicated whether there be firm or loose fibrous ankylosis or bony union.

For full description of Robin's osteo- and arthro-clasts see V. Robin, *Traitement du genou valgum à tous les âges par un nouveau procédé d'ostéoclasie mécanique*, 'Thèse de Lyon,' July 1882.

Also Édouard, *Du Redressement de l'ankylose du genou par de nouveaux procédés d'arthroclasie et d'ostéoclasie mécanique.* Thèse inspirée par V. Robin, Lyon, December 1882. J. T.

Whitman, R. The reconstruction operation for ununited fracture of the neck of the femur. *Surg. Gynec. & Obst.*, 1921, **32**, 479.

The author begins by stating as a general truth that results in fractures in general are determined primarily by efficiency of treatment in apposing displaced fragments and correcting deformity. The bad results of the treatment of fracture of the neck of the femur are due to inadequacy of the conventional treatment in these respects. Non-union is due to separation of the fragments. The only method of apposing the fragments is that of full abduction.

At the hip the range of motion is determined by the angle of the neck of the femur with the shaft; abduction is lessened by diminution of the angle. Coxa vara is the characteristic deformity resulting from 'extra-capsular fracture'; this causes actual and apparent shortening of the limb. Repair is slow, and the angle between the neck and the shaft causes greater strain on the bone in this position than is the case in other bones. Further, the joint is involved in a 'sympathetic arthritis', as evidenced by sensitiveness to weight-bearing and to passive movement, and by muscular spasm.

The primary deformity due to the fracture may be increased by permitting functional use before consolidation has occurred. Also if the injured part is subjected to strains which are beyond its powers the limb assumes the position of protection, namely, adduction and flexion.

Occasionally, fibrous union may produce stability, but there is usually a tendency to increase of the deformity and functional disability.

Operative treatment is the only one with a chance of removing the disability, but it has so far been confined to attempts to produce union of the fragments. Such an operation is practicable only if the neck be long enough to permit of abduction, and it is successful only if, after removal of all the fibrous tissue between the fragments, both fragments bleed freely. Under these circumstances if abduction and fixation by a bone peg be used, union is fairly certain. Further, had abduction been applied in the first instance operation would have been unnecessary.

In most cases this operation is impracticable because the neck has been almost absorbed. Also most of the patients are elderly people, with poor circulation. In the Mayo Clinic, in 120 cases of ununited fracture of the neck of the femur, operation was considered advisable in only 26, though most of the patients were physically favourable subjects. In only 10 (or 8 per cent.) was the functional result satisfactory.

Brackett has removed the extremity of the greater trochanter and implanted the inner surface of the upper end of the femur and trochanter into a hole cut in the head to receive it, but the disadvantage of this method is that success depends on the capacity of the tissues for repair. Other surgeons have removed the head of the femur and implanted the upper end of the femur in the acetabulum, possibly removing the great trochanter first so as to allow the bone to enter the acetabulum easily; this method has the disadvantage of complete loss of leverage by the abductors.

The author's procedure is as follows:

A half-U shaped incision is made from the anterior superior spine to three inches below the apex of the trochanter. The head of the femur is removed from the joint through the interval between the tensor vaginae femoris and the gluteus medius muscles. The trochanter is then removed with all its muscular attachments, and the upper end of the femur, having been remodelled, is thrust into the acetabulum, abducted at an angle of 25 degrees. The trochanter is then drawn downwards as far as possible and pegged or sutured to the freshened surface of the outer aspect of the shaft of the femur. After closure of the wound the limb is fixed in a long plaster spica for four weeks. The long plaster is replaced by a short one at the end of this time and the patient begins to walk. When there is no longer any pain the plaster is removed and exercises instituted to develop muscles. The author publishes six cases, five being women, aged from 52 to 60, and one a man, with tabes dorsalis, aged 45. All showed increase in movements and freedom from pain.

The author claims the following advantages for his operation:

(1) The removal of the trochanter restores a bearing surface and reconstructs a neck, which may be adapted to the acetabulum so as to make a stable articulation.

(2) Replacement of the trochanter at a lower attachment on the femur gives an effective leverage to the glutei for abduction.

He states his opinion that the immediate and efficient treatment of fracture of the neck of the femur by abduction will be usually followed by union. That if union does not occur the failure is due to a low vitality of the tissues, and therefore a reconstructive operation is to be preferred to a bone-grafting procedure.

He further suggests that his procedure is suitable for other cases in which there is destruction of the neck, as in arthritis deformans, and also for ankylosis from various causes. J. T.

Gaenslen, E. J., and **Thalhimer, W. Congenital syphilitic epiphysitis in adolescence.** *J. Orthop. Surg.*, 1921, **3**, 8–17.

This condition is usually described as occurring only during the first months of infancy. However, many cases of bone and joint syphilis in later life go unrecognized, and the great difference of opinion as to the frequency of these lesions is an index of our ignorance of the subject. The authors report a case of epiphysitis in which they have studied the pathology.

Description of case: Male, aged 13, with pain and lameness after fall on to the left hip. Febrile attack three months before with pain in the lower left extremity. Wasting of left thigh and leg with ½ inch shortening. The case was regarded as one of infantile paralysis. A year later patient returned with pain in the left hip and general indisposition. His temperature was 100° F., and he had limitation of movement of left hip with tenderness over left great trochanter. X-ray showed flattening and rarefaction of epiphysis of trochanter and of shaft. The Wassermann reaction was negative. The condition was regarded as a low grade infection and the trochanter was explored by turning it upwards after detaching it. The bone was seen to contain many areas of cartilage. A culture proved sterile.

The symptoms cleared up, but returned in about eight months. The Wassermann test now gave a positive reaction, and a history of syphilis in patient's father was obtained.

Description of specimen: Firm cortical bone. Cancellous bone more irregular than normal. Scattered areas of cartilage. This cartilage is of an embryonic type, with irregular arrangement of the cells. In the middle of some areas are islands of growing bone, whose edges are covered with osteoblasts. The age of the bone appears to vary in different parts of the section. In places the cartilage cells are arranged in lines exactly like those of epiphyseal cartilage. In other places there is excess of calcareous matter in it. The marrow spaces are filled with red and fatty marrow, but in some places there is an excess of connective tissue stroma. No dead bone is seen. The periosteum is considerably thickened, and its vessels show endarteritis.

The case was considered to be one of congenital syphilis on account of:

(1) Predominance of cartilage and active osteogenesis.

(2) Lack of completion of bone formation and excess of calcareous matter in the cartilage.

(3) Thickened periosteum and endarteritis. J. T.

Giannantoni, M. Sui 'tumori infiammatorii' degli arti. [**On 'inflammatory tumours' of the limbs.**] *Policlin.*, 1921, **28** (Sez. Chir.), 317.

Clinical notes of a case of massive 'tumour' of the thigh, of wood-like hardness associated with underlying osteoplastic osteitis, unaccompanied by symptoms. The mass was, apparently, not incised, but an inguinal gland was examined, and tested on a guinea-pig with negative results. The article alludes to a considerable number of cases in the literature, and gives a bibliography of sixty-two numbers. E. R. C.

Sorge, E. Sulla rigenerazione delle cartilagini costali. [**On the regeneration of costal cartilage.**] *Arch. ital. di chir.*, 1921, **3**, 481–506.

Experiments on dogs lead to the conclusion that loss of substance of cartilage, if the perichondrium be simultaneously removed, is made good by fibrous tissue; that at the margin of the lesion cartilaginous tissue is reproduced, but in very limited amount; new tissue is derived almost entirely from perichondrium, resulting from proliferation of the cells of its deepest layers; from them hyaline substance is derived; activity begins about the 4th day, is well-established from the 8th to 15th, and has ceased by the 28th. The very limited direct reproduction of cartilage is confined to the multiplication of cartilage cells, and seems to be not regenerative but purely cicatricial; connective tissue is not transformed into cartilage; sepsis, though it set up chondral and perichondral inflammation does not augment regeneration. E. R. C.

Henderson, M. S. Habitual or recurrent dislocation of the shoulder. *Surg. Gynec. & Obst.*, 1921, **33**.

Henderson reports on nineteen patients operated on in Mayo Clinic. He points out that it is difficult to find out how many patients whose shoulders are dislocated suffer from recurrent dislocation. The movements producing recurrent dislocation are abduction and a slightly forward movement of the arm.

The author's view is that recurrence is due to altered muscle tension; e. g. the infraspinatus and supraspinatus may be torn from their insertions. Also Lovett has described an abnormally large space between the head of the humerus and the acromion, suggesting relaxation of the capsule.

On the operating table the author has been able in only two cases to reproduce a dislocation; one was posterior dislocation. In view of the fact that recurrent dislocation is not produced by violent trauma the writer considers that it is not due to any bone deformity, but by action of certain muscles which thrust the head of the humerus against a weakened part of the capsule. When bony changes occur they are secondary.

Henderson believes that the factors producing recurrent dislocation are:

The primary accident causes a tear in the anterior inferior part of the capsule which is its weakest and laxest region. In this situation there is no tendinous support such as that given by the triceps below or the subscapularis above.

The supraspinatus and the infraspinatus may be torn, the ruptured part being replaced by scar tissue which stretches. Relaxation of these muscles permits the head of the humerus to drop into a lower position than the normal.

The teres major, latissimus dorsi, and pectoralis major tend to pull the head into the glenoid fossa, but also downwards and forwards.

The supporting action of the subscapularis is lost because the lowered position of the head causes this muscle to lie across the upper half of the head, leaving the lower half unsupported. As a result the head slips forward through the weak place in the capsule below the subscapularis, owing to the action of the teres major, pectoralis major, and latissimus dorsi.

The cases of 23 patients are reported, of whom 20 were males and 3 females; 2 were epileptics. The average age was 28. 19 were operated upon, but 3 too recently for estimation of the results. The operation performed was capsulorrhaphy. The anterior inferior weak part of the capsule was reinforced, as in Mayo's operation for abdominal hernia. In some cases the pectoralis major was lengthened.

Results:

No recurrence . . .	50 per cent.
Decidedly improved . .	31·25 per cent.
Failure	18·75 „ „

Patients operated on more than three years:

No recurrence . . .	37·5 per cent.
Decidedly improved . .	50 „ „
Failure	12·5 „ „

J. T.

Ansaldi, C. Sopra un tumore misto della guancia derivato da ghiandole salivare accessorie. [**On a mixed tumour of the cheek derived from an accessory salivary gland.**] *Policlin.*, 1921, **28** sez. chir., 277.

An exceptionally large tumour, weighing 75 gm. It had no connexion with Stenson's duct or with the anterior margin of the masseter. It was probably derived from one of the 'molar glands' described by Testut as lying between the buccinator and its fascia, or in the thickness of the muscle, arranged in a more or less continuous series reaching the palatine set; each opens by duct separately on the mucosa. Discussion of the histogenesis of 'mixed' tumours of salivary derivation. E. R. C.

JUDD, E. S. Jejunal ulcer. *Surg. Gynec. & Obst.*, 1921, **33**, 120.

This paper is a communication to the Association of Surgeons of St. Louis, and is founded on 101 operations for jejunal ulcer following gastro-enterostomy. Of the 101 cases, 55 had had the original gastro-enterostomy performed at the Mayo Clinic, 46 elsewhere. The ulcer is usually situated at the line of anastomosis—98 cases to 8 in the jejunum at a distance from the stoma. The efferent rather than the afferent loop is involved. From the frequency with which oedema and adhesions to surrounding viscera are met with, Judd concludes that a slow leak is common. Of 4,324 cases of gastro-enterostomy performed at the Mayo Clinic 55 were afterwards operated on for jejunal ulcer. These figures agree with those given by Paterson for the frequency of jejunal ulcer. Judd adds that no cases of jejunal ulcer have followed plastic operations on the pylorus, and that he has only seen one following partial gastrectomy for carcinoma, but gives no figures by which the relative immunity of these operations from the complication can be estimated.

Judd considers that a persistent high acidity of the stomach contents after gastro-enterostomy is the chief aetiological factor in the production of jejunal ulcer, a high post-operative acidity being present in over 60 per cent. of his cases. Next in order of importance is placed the use of non-absorbable suture material, which was found in 26 of the 101 ulcers examined at operation. He recognizes trauma as a possible cause, but is not impressed by its frequency and does not consider that the blame so frequently attributed to the use of clamps during the performance of the anastomosis is, in reality, justified. While admitting that infection must play some part in the production of jejunal ulcer, he does not think it necessary to assume that this infection is derived from the original gastric or duodenal ulcer for the relief of which gastro-enterostomy was performed, as he considers it questionable if infection carried to the freshly-cut surfaces would result in the same type of lesion. Moreover, he notes that in 15 of the 101 cases there was no evidence that an ulcer of stomach or duodenum had ever existed.

Among his cases were 6 of gastro- or jejuno-colic fistula, but these are not discussed in detail. He suspects jejunal ulcer in all cases of recurrence of symptoms after an interval of relief following the gastro-enterostomy, and for diagnosis relies chiefly on the X-ray findings of deformity of the stoma and narrowing of the jejunum in its immediate neighbourhood.

Judd considers medical treatment unsatisfactory, and in his operative treatment relies for prevention on avoidance of trauma and of the use of non-absorbable sutures at the original gastro-enterostomy and on strict adherence to a suitable post-operative diet. His standard method of treatment of jejunal ulcer is to undo the gastro-enterostomy, excise the ulcer, and perform pyloroplasty. It is his experience that anastomosis ulcers frequently reform if the original gastro-enterostomy is reconstituted after excision of the jejunal ulcer. A table of the cases operated upon at the clinic from 1912 to 1921 is appended. E. K. M.

Palmer, D. W. Duodenal ulcer in infancy. *Ann. Surg.*. 1921, **73**, 545.

Palmer reports one case of duodenal ulcer in a boy of six months. The symptoms were vomiting and wasting and there was no delay in evacuation of the stomach contents as shown by X-ray examination. The pre-operative diagnosis was hypertrophic stenosis of the pylorus. Treatment by pyloroplasty, followed eighteen days later by posterior gastro-enterostomy, was entirely satisfactory, the child being healthy and up to normal weight at the age of two years.

In a brief review of the literature Palmer gives the average age of the patients as three and a half months. The chief symptoms are pain, vomiting, and wasting, with haemorrhage as a terminal symptom of grave prognostic significance. The recorded cases have not been associated with burns.
E. K. M.

Rosenow, E. C. Focal infection and elective localization of bacteria in appendicitis, ulcer of stomach, cholecystitis, and pancreatitis. *Surg. Gynec. & Obst.*, 1921, **33**, 19–26.

Rosenow has for some time been working on the elective localization of bacteria in certain diseases, and has come to the conclusion that many inflammations of organs such as the appendix, stomach, pancreas, gall-bladder, hitherto usually regarded as due to infection from neighbouring surfaces, may really be blood-borne from distant foci. In favour of this view he adduces the following arguments:

1. The early lesions of these organs are often sharply defined, haemorrhagic, and situated in any of the coats, without necessary involvement and infiltration of the mucous membrane.
2. He has caused infections of the pancreas by intravenous injection of bacteria and found them localized chiefly in the pancreatic head, just as much as in the usual clinical cases, in which this localization was supposed to be an indication of spread up the ducts.
3. Experimental feeding of animals with streptococci, even when mixed with sharp particles, failed to induce gastric ulcer except in starving animals; yet intravenous injection of these streptococci caused ulceration of the stomach.

Streptococci injected directly into the gall-bladder did not produce cholecystitis, but when injected into the blood-stream did so. He also found that streptococci from acutely diseased appendices, when injected into the veins of rabbits, caused appendicular lesions, whereas their introduction via the mucous membrane failed to act in this manner, unless the blood-supply of the organ had been materially damaged. He suggests that in many cases the infection is blood-borne and that the decision as to the site of damage depends on the elective affinities of the organism travelling in the blood but probably originally derived from some distant focus, such as teeth, tonsils, &c.

He regards various streptococci as the chief offending organisms in these cases, chiefly of the non-haemolytic type and of a low grade of virulence; these varieties are culturally much alike but are differentiable by their behaviour on intravenous injection; they showed a specific selection in that the micro-organisms taken from an appendicitis tended to produce appendicular lesions in the injected animal, those from gastric ulcers caused stomach lesions, and so on.

He states that streptococci found in teeth sockets, tonsillar crypts, &c., although apparently alike, yet possess these elective powers, so that one strain may, on injection into the blood-stream of animals, habitually cause appendicitis, whilst another will persistently produce cholecystitis, another gastric ulcer, and so on. 'It appears that the bacteria acquire elective localizing power in the focus and that the various diseases may be manifestations of phases of the infecting power of the same micro-organism.'

His previous experiments on these lines were objected to because of the large doses of organisms injected and because other workers failed to corroborate; therefore he has now performed a much larger number of experiments, using smaller doses.

His results are set out in tabular form thus :

Elective Localization of Streptococci in Gastric Ulcer, Cholecystitis, and Appendicitis.

Source of Streptococci.	Strains.	Animals.	Percentage of Animals showing Lesions in :															
			Eyes.	Teeth.	Skin.	Muscles.	Joints.	Intestines.	Appendix.	Stomach and Duodenum.	Gall-bladder.	Kidneys.	Lungs.	Pericardium.	Myocardium.	Endocardium.	Nerves.	Central Nervous System.
Ulcer of stomach	37	168	0	4	0	4	12	4	1	**68**	21	3	0	2	3	10	0	?
Cholecystitis	12	41	0	0	2	7	17	17	0	29	**80**	5	5	0	2	10	0	?
Appendicitis	17	71	0	0	0	12	29	9	**70**	11	1	0	0	0	9	21	0	?
Myositis	24	159	0	7	3	**75**	31	0	0	15	2	11	7	6	14	11	11	?
Acute Poliomyelitis	24	123	0	2	0	16	15	5	2	13	2	2	11	5	7	7	4	**46**
Miscellaneous	71	212	4	3	4	12	9	4	1	9	1	9	7	0	4	12	4	?

His experiments appear to justify his claims as to the selective infectivity of strains of streptococci : he also emphasizes the possibility of the presence of organisms of these special localizing selectivities collecting in teeth sockets, tonsils, &c., and their tendency to cause the disease of their affinity.

The subject is an important one to the surgeon, and it is to be hoped that it will be submitted to further examination by other investigators.

C. C. C.

Larrieu, J.-E. La perforation de l'ulcère gastrique après la gastro-entérostomie. [**Perforation of gastric ulcer after gastro-enterostomy.**] *Rev. de chir.*, 1921, **59**, 278.

In 10,500 collected records of gastro-enterostomy for simple ulcer of the stomach, Larrieu found 81 cases of perforation, exclusive of perforation of anastomosis or jejunal ulcer. In 30 of the 46 cases in which the date of perforation after the gastro-enterostomy was noted it occurred in the first month. Larrieu concludes that it is almost always the old, adherent ulcers which perforate, and that the chief factor in production of the perforation is the forcible separation of adhesions which is apt to be carried out in the performance of a difficult gastro-enterostomy.

The diagnosis of perforation presents no difficulties if it occurs late, but when it happens during the early days of convalescence after the gastro-enterostomy it may readily be mistaken for acute dilatation of the stomach. The chief points of difference are that in perforation there is usually a rise of temperature, which is absent in acute dilatation, and that the vomiting which accompanies both conditions yields easily to treatment by lavage and posture in the case of acute dilatation, but is unaffected in perforation. With the development of peritonitis retraction of the abdominal wall is a significant sign, in contrast to the distension associated with acute gastric dilatation. E. K. M.

Lewis, R. M. Cancer of the ampulla of Vater. *Surg. Gynec. & Obst.*, 1921, **32**, 543–6.

Robert M. Lewis, of Baltimore, reports a case of adenocarcinoma of the ampulla of Vater which had been successfully removed by Howard A. Kelly and Curtis F. Burnam 8½ years previously. The patient had been suffering from jaundice for two months and flatulent indigestion for two years. The abdominal pain and distension was of ill-defined type, with no special reference to time, quantity, or quality of meals. The faeces at the time of operation were constipated and clay-coloured, and the urine was loaded with bile. At operation (March 1910) the gall-bladder and common bile-duct were found to be dilated, a fixed hard nodule could be felt through the duodenum in the position of the ampulla. Exploration of the duct failed to demonstrate any stone; therefore the duodenum was mobilized and longitudinally incised, whereupon the mass was found to be a hard, white nodule of carcinomatous appearance at the ampulla. The nodule and duct were pulled forward into the gut, and were excised, the divided end of the bile-duct being re-implanted into the duodenum and fixed there with catgut sutures. The openings into the duodenum were closed, also that made into the common duct for exploration. Drainage was secured through the gall-bladder and also by a cigarette drain down to the closed opening in the common duct.

Convalescence was uneventful.

Microscopic examination (Dr. Burnam) showed the growth to be an adenocarcinoma of the ampulla of Vater.

When seen by Lewis in July 1919 the patient was in good health and had entirely lost her symptoms.

Comparatively few similar cases have been recorded. Upcot (*Ann. Surg.*, 1912, **56**, 710) collected sixteen cases of radical operation for this condition, in only three of which was operative recovery recorded.

Kausch reported another success (*Zentralbl. f. Chir.*, 1909, **36**, 1350), and expressed the belief that the prognosis of the operation should be good because definite symptoms arise early and so lead to timely diagnosis and treatment before metastasis has occurred.

Diagnosis is, however, rarely made before laparotomy has been performed. Cordua (*München. med. Wchnschr.*, 1906, **53**, 2324) and Oehler (*Beitr. z. klin. Chir.*, 1910, **69**, 726) both draw attention to jaundice, chronic constipation, and distension of the gall-bladder as cardinal symptoms, and the latter writer draws attention to pain in the region of the gall-bladder with absence of fever or colic as confirmatory and suggestive symptoms.

The character of the growth has proved to be an adenocarcinoma in the examined cases.

The type of operation adopted has varied with different surgeons and with the stage of the disease. For radical cure in a case without serious secondary growths excision of the part of the duodenal wall bearing the tumour, followed by re-implantation of the bile-duct into the duodenum, and by biliary drainage via the gall-bladder, as adopted in Kelly and Burnam's case, seems to be the best plan. Halsted and others removed part of the duodenum and of head of pancreas and transplanted the common bile-duct and pancreatic duct into the duodenum. Cholecystenterostomy may be required if implantation of common bile-duct into the duodenum be found to be impossible. In many cases gastro-enterostomy was performed, and on theoretic grounds it would seem advisable to the abstractor that this short circuit should be made in order to give comparative rest to the region of the duodenal excision, especially if any fear remain in the mind of the operator that secondary cicatricial stenosis may follow an extensive removal of duodenal wall.

For palliative treatment alone a gastro-enterostomy and cholecystenterostomy have chiefly been done. C. C. C.

Crescenzi, G. A proposito di un caso di ernia del Treitz strozzata. [**Strangulated hernia of Treitz.**] *Arch. ital. di chir.*, 1921, **3**, 421.

A case of successful operation for a typical case of hernia duodenale sinistra. There had been several attacks of severe abdominal pain with obstinate constipation relieved by enemata. In the attack which necessitated operation there was a tumour in the left side of the abdomen, limited by the mid-line, the costal border, and interspinous plane. This tumour could be felt to become tense at intervals of some seconds—with a sensation like that of the contracting gravid uterus, and corresponding with the colicky pains. When present such clinical signs are highly suggestive of the diagnosis. The loops within the sac were easily withdrawn and no damage had been done by the taut margins of the orifice of the sac. Obliteration of the sac by excision, by drainage from a dependent point, is desirable. Closure of the orifice is difficult or not feasible. Division of the outer border, if it be essential to relieve strangulation, is not necessarily fatal, for the inferior mesenteric vein is probably thrombosed and the left colic artery has plenty of arcading anastomoses. In the author's case there was a very marked dilatation of the veins in the lower abdominal wall and upper part of the thighs; the significance is discussed. It is possible that in the formation of the sac, which has sometimes several folia, retro- or para-colic pouches or blind sacs of developmental origin take a part. E. R. C.

Bianchetti, C. F. Considerazione sopra un caso di ernia inguinale interna nella donna. [**On a case of internal inguinal hernia in the female.**] *Policlin.*, 1921, **28** (Sez. Chir.), 309.

Clinical description of a case with an account of the minute anatomy of the abdominal wall in the region of the inguinal canal, including that of Donati's 'lamina pubo-transversalis', an aponeurotic structure lying in front of the fascia transversalis between the transverse aponeurosis and the conjoined tendon, immediately external to the rectus muscle and sometimes also in front of it; it is inserted below into the pubes with Gimbernat's ligament and runs upwards vertically towards the transversalis. It is to be distinguished from Henle's 'falx inguinalis'. E. R. C.

Möller, H., og **Wessel.** Prolapsus recti hos börn behandlet ad m. Ekehorn. [**Ekehorn's operation for prolapse of the rectum in children.**] *Hosp.-Tid.*, 1921, **64**, 8.

Möller criticizes the conservative treatment of prolapse of the rectum in childhood with sticking plaster, for though the ultimate results may be good, it requires much time, and on account of its lack of cleanliness it is difficult to carry out in the patient's home. Thiersch's operation and its modifications have given good results, but they are apt to be followed by complications. Möller has performed Ekehorn's operation in 15 cases with immediate good results and without complications other than insignificant stitch abscesses. In 12 cases the patients were re-examined, and the recovery found to be maintained. The operation is to be recommended as being effective, safe, and quickly performed; it also requires only a short stay in hospital. The operation consists of fixing the posterior wall of the rectum to the sacrum by a transverse suture. No incision of the skin or rectum is required. The prolapsed rectum having been replaced and kept in position by the forefinger of the left hand, a moderate-sized needle on a handle is passed through the skin to one side of the extremity of the sacrum. It is carried through the soft tissues till it pierces the rectum and meets the finger which guides it to the anus. The needle is now threaded with stout silk, one end of which is drawn back with the needle. By a similar procedure the other end of the ligature is brought out at the same level on the other side of the sacrum. The two ends of the ligature are now tied together over the skin. No dressings are required, and the patient need not be kept in bed. The suture is removed after a fortnight.

Wessel recommends Tuttle's rectopexia sacralis, the result of which was excellent in the case of an adult operated on in 1907 for an 18 cm. long prolapse. Soon afterwards an infant whose prolapse had lasted a year was treated on the same lines but less radically. A large Hagedorn needle, threaded with a silk suture, was inserted to one side of the upper portion of the coccyx, and, guided by the left index finger in the rectum, was carried through the posterior wall of the rectum without the mucous lining being involved. Having traversed the submucous tissues of the rectum, the needle was brought out again at the same level but at the other side of the coccyx, and the two ends of the suture were united over a small pad of gauze. By avoiding the mucous layer of the gut, Wessel believes he has rendered the operation comparatively aseptic, whereas Ekehorn's operation is apt to lead to stitch abscesses. At the Bispebjerg Hospital, Wessel has treated 18 cases of prolapse in children, 4 being mucous and 14 rectal. In 2 of the mucous and 9 of the rectal prolapses operative treatment was adopted, and the operation described was performed in all but 2 of these cases. Relapses occurred in 3 cases, and were traced to the fixation of the gut being below the level of the inverted section. Success was achieved by re-operation, which in one case was Ekehorn's. Suppuration followed, but the ultimate result was satisfactory. With regard to the technique of Wessel's operation, a gigantic Hagedorn's needle is required when the inversion of the gut is at a high level and the child is several years old.

C. L.

Whipple, A. O. The use of the duodenal tube in the pre-operative study of the bacteriology and pathology of the biliary tract and pancreas. *Ann. Surg.*, 1921, **73**, 556.

Whipple has examined cases presenting various lesions of the biliary tract by means of the duodenal tube and compares the data obtained with the findings at the subsequent operation. He tabulates the pre-operative and post-operative results of bacteriological cultivation of the bile (25 cases), finds that in about 50 per cent. of the cases one or more varieties of bacteria found in the pre-operative duodenal bile were present in the gall-bladder bile or wall, points out the frequency of contamination with organisms of oral origin, and draws no conclusion other than that *B. coli* is the most persistent of the bacteria found in the common duct. In 26 cases he compared the activity of the pancreatic ferments recovered from duodenum before operation with the condition of the pancreas as determined at the laparotomy, but was unable to find any correlation between the two which could be considered of diagnostic value.

In 27 cases he compares the flow of bile from the duodenal tube before and after injection of $MgSO_4$ (25 per cent. solution) into the duodenum with the condition found at operation, and concludes that the rate of flow and character of the bile is of definite value in diagnosis of the type of lesion present in the biliary apparatus. The object of the injection of $MgSO_4$ is to cause contraction of the walls of the gall-bladder and relaxation of the sphincter at the lower end of the common bile-duct, but, as experimental confirmation of the correctness of this hypothetical action is, at present, wanting, any conclusions founded upon it must remain a matter of conjecture. E. K. M.

Evans, A. Cystic adenoma of the bile-ducts. *Brit. J. Surg.*, 1921, **9**, 155 and 156.

Arthur Evans reports a case of this rare condition in a woman aged 53. She had complained of pain in the upper part of the abdomen for one year, with occasional vomiting. She was slightly jaundiced and suffered from constipation, but had had no haematemesis or malaena. When examined she was emaciated and looked ill and was suffering from constant pain in the upper abdomen. The edge of her liver was palpable below the costal margin and continuous with it was a smooth rounded tumour, dull on percussion and fixed posteriorly. Examination of the urine, faeces, and the stomach contents revealed nothing of note.

Her blood contained 13,700 leucocytes per c.cm., apportioned as follows:

Polymorphs	Neutro-	75
	Eosino-	1
Monomorphs	Large	5
	Small	18
Transit		1
		100

Her Wassermann test was negative.

At operation a large cystic swelling was found attached to the under surface of the liver over an area of about six inches and passing back into the right paravertebral fossa. It was believed to be a hydatid cyst and opened, but no daughter cysts were found. The contents were removed as much as possible and a drainage-tube inserted.

Pathological examination was made by Braxton Hicks. The cyst was lined with well-formed non-ciliated columnar cells which could be seen secreting mucin. The interstitial tissue between the cysts was a coarse fibro-muscular tissue. His decision was that the tumour was a multilocular cystic adenoma arising from bile-ducts.

The condition is a very rare one, but cases have been reported by Walker Hall and Brazil (*Med. Chron.*, Manchester **6**, 233) Keen (*Boston M. & S. J.*, **126**, 405), Ziegler (*Path. u. Anat.* 606). C. C. C.

Ballin, M. A method of cranioplasty using as a graft one-half of the thickness of the bony part of a rib. *Surg. Gynec. & Obst.*, 1921, **33**, 79–83.

Max Ballin, of Detroit, described in detail a method of closing cranial bony defects by the use of split ribs, after the insertion of a sheet of pectoral fascia superficial to the dura and deep to the bone. He points out that in adults cranial defects show no tendency to repair, although the periosteum, the dura, and diploe all have osteogenetic powers; the exposed meninges or brain substance tend to become adherent to the overlying skin, so preventing or limiting the spread of new bone formation across the gap. Some method of closing the gap is frequently called for by the presence of unpleasant symptoms which chiefly show themselves in the form of:

(*a*) Constant and severe headache.

(*b*) Perversion of disposition, often associated with melancholia, insomnia, and emotional disturbances, and frequently exaggerated by the weather changes, heat, exertion, &c.

(*c*) Vertigo or nausea, especially when changing position suddenly, or experiencing vibrations, such as those of a train or motor-car.

(*d*) Sense of cranial insecurity.

(*e*) Epilepsy in a certain proportion of cases.

Cranioplasty relieves many of these symptoms, often immediately.

The use of foreign bodies such as silver, celluloid, paraffin, and so on, has been entirely abolished; heterogeneous grafts have also been given up.

The Koenig-Mueller method of cutting two pedunculated flaps (one containing the scalp covering the defect and the other consisting of scalp, pericranium, and outer table from healthy bone in the neighbourhood), and then exchanging them so that the bone-containing flap covered the defect while the boneless flap took the place of the former, has certain advantages but some very present disadvantages, e. g. (1) haemorrhage from scalp and diploe during the operation; (2) buckling of the pedicles during exchange of the flaps; (3) the spongiosa is laid directly upon the dura, a proceeding which tends towards callus formation and subsequent cortical irritation.

The Hacker-Durante modification of the Koenig-Mueller method involved taking a flap of periosteum and outer table and then turning on its own pedicle so that the periosteal surface was laid next the dura. The disadvantages of this method are that (1) the flap is not easy to make; (2) the repeated hammering necessary sometimes caused cerebral concussion; (3) the flaps were liable to gangrene.

Morestin introduced cartilage grafts as being more easily fashioned to the circumference of the cranium than is bone. The immediate results are good, but there have been several instances of absorption of the graft;

therefore autogenous bone transplantation is now the method of choice. Morestin bevelled off half an inch at opposite edges of the defect to make a bed for the graft, and held this graft in position by sutures through holes bored through the inner table.

Nesselrode took the ends of the graft in between the inner table and the dura.

Gallie and Robertson first suggested half the thickness of a rib as the graft: they did this for the mandible, but Ballin has used the same graft for the skull. His method is as follows:

(1) A flap incision is made over the sixth and seventh ribs in the mid-axillary region.

(2) A quadrilateral piece of fascia, rather larger than the skull defect, is excised and placed in warm saline solution.

(3) The muscles are pushed back so as to expose the ribs, then with a thin narrow chisel the outer half of each rib is split off, leaving the inner half intact. Each piece should be a little longer than the width of skull defect to be closed. Each piece of rib, as cut, is put into saline solution until required, and the thoracic wound is sutured.

(4) The skull defect is exposed through a quadrilateral flap incision. The skin is carefully dissected off the underlying adherent dura and brain. The dura is freed from the bony edge of the defect and then, with a chisel or nibbling forceps, the bony edge is cut away evenly for a quarter of an inch all round, and the corners of the gap are squared.

(5) The fascial square is now smoothly laid in, superficial to the brain and dura, and tucked under the bony edges of the defect.

(6) By light strokes of a chisel into the cancellous diploe, a groove is made all round between the outer and inner tables of the skull.

(7) The split-rib grafts are now bent between the fingers with the aid of forceps grasping their middles, and are, one after the other, inserted into the grooves made for them. Their own elasticity will keep them in place, with a slight convexity away from the brain, if they have been cut a little longer than the width of the gap.

The advantages of the operation are:

Both fascial and bone grafts are obtained from the same place; the pectoral fascia, being light and covered with some fat on each surface, is less likely to adhere than a flap cut from the tougher fascia lata; the rib is easily split and, the inner half being left, avoids a serious thoracic defect; the half-rib graft is flexible and readily bent to adapt itself with a curve to the skull gap; the slot in the edge of the skull defect is easily made and holds the rib graft firmly mortised.

Brown (*Med. J. Australia*, 1917) has described a method of inserting rib grafts into skull gaps, but he had not added the transplant of fascia and had fixed his rib by a lattice of sutures. C. C. C.

Foley, F. E. B. Clinical uses of salt solution in conditions of increased intracranial tension. *Surg. Gynec. & Obst.*, 1921, **33**, 126.

Since the brief review on the experimental alteration of brain volume in *Medical Science* (1921, **4**, 535) a further detailed paper on the clinical application of the methods then described has been published by Foley. He finds that in the human subject gastro-intestinal doses of hypertonic saline solution produce the same reduction in cerebrospinal pressure and brain volume as intravenous injections. The cerebrospinal pressure was recorded by means of a normal saline manometer connected with the subarachnoid space by lumbar puncture. The patient was then given 16 gm. of sodium chloride by mouth in capsules, or 190 c.cm. intravenously in 15 per cent. solution. In one case an initial pressure of cerebrospinal fluid of 200 mm. saline rose during injection to over 240 mm. and then fell rapidly to below 120 mm. within the hour. In patients in whom decompression operations had been performed a simultaneous shrinkage and softening of the brain protrusion was seen. This shrinkage was greatest in cases of internal hydrocephalus, and was not remarkable in increased intracranial tension apart from this. It was measured by means of an air tambour applied to the bony opening in the skull and connected with a water manometer ; the method being that employed by Ebaugh and Stevenson. Foley explains the results as follows: the increased osmotic value of the blood produced by the salt promotes the absorption into the circulation of fluid from the subarachnoid space, while the rate of secretion by the choroid plexuses is diminished. A marked lowering of intracranial tension follows. He suggests an explanation of the mechanism of increased intracranial tension. With internal hydrocephalus, the brain is pressed against the cranium, and the escape of cerebrospinal fluid through the arachnoid villi (*Medical Science*, 1920, **3**, 160) cut off by the closure of these. The fluid is now under increased tension. Absorption takes place in the reverse direction through the choroid plexuses into the blood-stream, and a fall in tension results. In the case of tumour mass without hydrocephalus, the same closure of the channels of absorption may occur, but now the enlarged and compressed brain can shrink only by dehydration, since the ventricles contain relatively little fluid. In the circumstances, therefore, salt ingestion would, as is in fact the case, have little result. Foley concludes that the procedure has a definite clinical usefulness, which has not yet been fully explored. In increased tension due to hydrocephalus, the obstruction to cerebrospinal escape is the primary cause of the increased intracranial tension and is directly relieved by salt ingestion. In cases of actual increase of brain bulk from tumour, without hydrocephalus, but little reduction follows. Possibly it may be of use in relieving obstruction to fluid outflow in cases of meningitis. Practically, the administration of salt solutions is the most valuable weapon we possess for the relief of 'pressure headaches'. Lumbar puncture is much safer after this procedure, while general anaesthesia for operative measures is facilitated by a preliminary reduction of intracranial tension. Possibly also certain cases might be tided over periods of acute pressure, though this has not been confirmed by actual experience. F. M. R. W.

Dandy, W. E. An operation for the removal of pineal tumours. *Surg. Gynec. & Obst.*, 1921, **33**, 113–20.

Dandy, recognizing that tumours in the pineal region are becoming more diagnostically localizable, has followed up his previous operative manœuvres on the pineal body in dogs by devising and practising a similar procedure in man. He has performed this operation on three patients ; in the first he found an irremovable cerebellar tumour that had infiltrated the pineal body and corpora quadrigemina ; from the other two he successfully removed the pineal tumours.

One of these was a hard, nodular, perfectly encapsulated mass measuring 5 cm. by 4 cm. The patient recovered without untoward mental or physical effects, but died eight months later. Although the gross appearance of the tumour was that of an endothelioma, microscopic examination proved it to be a tubercle, and it is presumed that the patient's subsequent death was due to other cerebral tubercles ; no necropsy was obtained.

The other tumour was much larger, and weighed 26 gm., it was hard, fairly nodular, and perfectly encapsulated. Its extirpation was difficult owing to its extensive vascular attachments ; the vena magna Galeni and both small veins of Galen passed through it ; but these were finally secured and removed, and the tumour was then readily lifted from its bed. This patient died 48 hours after operation, presumably from shock due to the severe operation, which had followed a cerebellar exploration done ten days previously. The removal of the veins of Galen may have been a contributory mortal factor, although Dandy has ligated the vena magna Galeni in dogs without fatal result.

The operation has the following steps :

(1) A very large right-sided parieto-occipital bone flap is made, with its mesial border extending to the superior longitudinal sinus ; at this stage there may be considerable haemorrhage from the venous lakes urgently demanding effective haemostasis.

(2) The dura mater is then opened and reflected over the inferior longitudinal sinus, the cerebral veins in the subdural space being divided between double fine silk ligatures. The Rolandic vein should be divided to diminish the risk of hemiplegia and the right side of the skull should be attacked, lest aphasia follow.

(3) The whole posterior half of the cerebral hemisphere can then be retracted and in turn the falx, the inferior longitudinal sinus, and the corpus callosum are exposed.

(4) The posterior half of the corpus callosum is then carefully incised in the mid-line for about three or four cm., and the hemispheres still further retracted until the tumour is in good view. The vena Galeni magna is always seen at its entrance into the sinus rectus, under the fornix of the corpus callosum.

(5) The tumour is then enucleated from its bed on the roof of the third ventricle ; in one case it came away readily from the vena Galeni, in the other this vein had to be doubly ligated and divided.

An important accessory step is the early puncture of the lateral ventricle to allow an escape of the excess of fluid from the internal hydrocephalus that is always a feature in these cases, and is no doubt due to the occlusion of the aqueduct of Sylvius by the pressure of the tumour. The description of the operation is admirably illustrated by Broedel.

C. C. C.

Roello, G. Su un caso di linfangioma della regione temporale. [**On a case of lymphangioma of the temporal region.**] *Arch. ital. di chir.*, 1921, **3**, 453–69.

A study in histo-pathogeny pursued as a contribution to the aetiology of tumours and suggesting that differentiation of embryonal tissue may be postponed, or imperfect, or, once complete, may not be maintained.

E. R. C.

NEUROLOGY

Ramsay Hunt, J. The static or posture system and its relation to postural hypertonic states of the skeletal muscles, spasticity, rigidity, and tonic spasm. *Neurol. Bull.*, 1921, **3**, 207.

Ramsay Hunt here develops a theory already put forward in an earlier paper, which has been reviewed in *Medical Science* (1920, **2**, 272). He believes that the efferent or motor system is dual, both anatomically and functionally. The two motor systems, kinetic and static, normally co-operate to effect perfect motor co-ordination, but disease may dissociate the two elements, much as Head believes to be the case with cutaneous sensibility. Movement is a function of the kinetic system, while the adoption and maintenance of postures is subserved by the static system. The muscular contraction underlying posture is paradoxically described as 'a more passive form of contractility' than that which occurs in movements. Certain speculations now current as to the relations of the anisotropic disks and the sarcoplasm of the muscle-fibre to movement and posture respectively are quoted with approval. Both movement and posture may be subdivided into reflex, automatic-associated, and isolated synergic types. Underlying these three main types of motor activity are three fundamental divisions of the nervous system: *the segmental nervous system*, containing the great reflex arcs of the neuraxis; *the palaeo-encephalon* represented by the corpus striatum and optic thalamus, which are the higher co-ordinating motor and sensory centres of lower forms of animal life; and *the neo-encephalon*, which is the latest product of evolution and governs the highest motor and sensory activities. Each motor system is again subdivided into two components, neo-kinetic and palaeo- or strio-kinetic, and neo- and palaeo-static. In effect, though Ramsay Hunt does not say so, the efferent system is quadruple according to his hypothesis.

The pyramidal, neo-kinetic system regulates isolated-synergic movements, while the strio-kinetic is responsible for automatic-associated movements. Purely reflex movements are presumably a function of the segmental nervous system. The cerebellum is the essential integrating and correlating mechanism for the three aspects of postural activity. The vermis system, or palaeo-cerebellum, receives its afferents from the spinal cord; the lateral lobes, or neo-cerebellum, from the cerebral cortex via occipito-temporo- and fronto-pontine paths which reach the crossed lateral lobe by the middle cerebellar peduncle. The efferents of the two systems are, in the case of the neo-cerebellar system, dentate nucleus, superior cerebellar peduncle, nucleus parvo-cellularis of red nucleus; in the case of the older system, roof nuclei, superior peduncle, nucleus magno-cellularis of red nucleus. From this, both descend the cord 'in the rubro-spinal and other systems', and thence reach the muscles by separate peripheral systems.

In the case of both movement and posture there is no hard and fast line between the three types, and each system partakes in some measure of the functions of the other. How this is possible, with the definite anatomical basis of each which is postulated, we are left to discover.

Hunt believes that both postural arcs pass through the cerebellum, and in accordance with the generally accepted view that this organ acts subconsciously, is the subconscious nature of all postural activities.

With this as his physiological and anatomical ground-work, Hunt proceeds to the clinical application of the theory. He does not achieve this without some contradiction, and we are met at the outset with the statement that a lesion of the higher levels of the kinetic system releases lower level kinetic mechanisms from control and postural hypertonus results. In other words, the release of kinetic mechanisms produces postural over-action. Many different types of postural hypertonus are described: the spasticity of pyramidal tract lesions, the rigidity of paralysis agitans, decerebrate rigidity of mid-brain transection, and the postural hypertonus of pontine and more caudal lesions. Paralysis of the neo-kinetic mechanism releases the 'neo-spinal kinetic system', and presumably also lower level static systems, so that increased tendon-jerks and postural fixation of the limbs develop. Lesions of the palaeo- or strio-kinetic mechanism release only brain-stem centres, spinal centres being still under control. Therefore there is no alteration of tendon reflexes and isolated-synergic movements remain, but automatic-associated movements are lost, and there is rigidity and a characteristic form of postural fixation (due to release of brain-stem centres). Combined pallido-pyramidal types of motor disorder also exist. Decerebrate rigidity is said to result from lesions producing the effects of transection of the brain-stem anterior to the superior corpora quadrigemina. Kinetic and static mechanisms in the mid-brain and pons are released in this way. The rigidity is 'reflex standing', and is due to the activity of the palaeo-cerebello-rubro-spinal system. Lesions caudal to the red nucleus abolish it.

The paper contains so many unfounded anatomical and physiological assumptions that an adequate analysis of it is not possible within a small compass. However, a few of the more debatable points may be briefly mentioned. We are told nothing of the final integration of the activities of the kinetic and static systems. Leaving aside the extreme improbability that four separate and clear-cut mechanisms of the kind postulated by Ramsay Hunt exist, we may ask what are the functions of the motor cortex and its projection system under the conditions of this theory? We can hardly correlate the conclusions of Sherrington and Leyton on this point (*Medical Science,* 1921, **3,** 349) with Hunt's restricted view of cortical activity. There cannot be any hard and fast distinction between kinetic and postural systems, and the motor cortex appears to influence both types of motor activity. Moreover there is some evidence that changes of posture, that is, movement, may sometimes be the result of inhibition of postural contraction, and not that of the intervention of some distinct nervous mechanism. It is difficult to understand, also, why release of lower level kinetic mechanisms should lead to postural hypertonus, tonus being a function of one or other of his static systems.

Further, while there is much that is attractive in the conception that the cerebellum integrates postural activities in the manner described, the conclusion is not justified in the present state of knowledge. Ramsay Hunt deprecates the drawing of conclusions from animal experiment in respect of the forms of hypertonus observed in man. He may well do so, for it is by this means alone that he can be brought to book for the more extravagant of his speculations. His views on the cerebellum afford a case in point.

There has always been some doubt as to whether decerebrate rigidity could occur after extirpation of the cerebellum. Experiments of Sherrington, Horsley, Thiele, and Weed suggested that it may. In four papers of fundamental importance in this connexion ('Beiträge zum Problem der Körperstellung,' *Arch. f. d. ges. Physiol.*, 1916–18), Magnus records discoveries that cut the ground from under almost all Ramsay Hunt's physiological hypotheses. He finds that decerebrate rigidity only occurs when the plane of transection lies in the caudal half of the mid-brain, that is, caudal to the red nucleus. It develops equally well after extirpation of the cerebellum. Further, all the postural reflex reactions of the animal, rabbit, cat, or dog, are intact after section through the brain-stem immediately anterior to the superior corpora quadrigemina. Such a mid-brain preparation can not only stand in a variety of postures, but if overturned can right itself. It can also run and jump. The majority of the component reactions concerned are independent of the cerebellum, and are seen equally well after extirpation of that organ. Here strio-kinetic, neo-static, and palaeo-static systems have all been removed, but posture and automatic-associated movements are intact.

On the anatomical side, also, it is doubtful whether there is any sanction for the liberties he takes with the structure of the nervous system. We are not aware of any evidence relating the supposed neo- and palaeo-static cerebellar systems with the nuclei parvo- and magno-cellularis respectively of the red nucleus, nor does Ramsay Hunt afford any. So rich is the central nervous system in tracts and cell stations, that it is an easy task to string them together in the construction of hypothetical motor systems, but a list of tracts and nuclei is not necessarily a physiological pathway. If it were, and there is some reason to believe that the idea is a popular one, the rubro-spinal tract must be the most shamefully over-worked tract in the central nervous system, to judge by the number of functional combinations and permutations in which it is to be found in clinical neurological literature. F. M. R. W.

Hassin, G. B. The contrast between the brain lesions produced by lead and other inorganic poisons and those caused by epidemic encephalitis. *Arch. Neurol. & Psychiat.*, 1921, **6**, 268.

The term encephalitis has been used to include the brain lesions due to organic and inorganic poisons as well as those produced by infections, such as general paralysis, trypanosomiasis, epidemic encephalitis, and poliomyelitis. Hassin believes that these two groups of cases, infective and toxic, produce distinct and characteristic lesions.

For the study of toxic encephalitis he has obtained material from three cases of lead poisoning, one acute and two of longer standing, while in the case of arsenical encephalitis he has investigated the brain lesions experimentally produced in monkeys by salvarsan injections. The lesions are parenchymatous and interstitial. The nerve-cells show degenerative changes, which are not typical for the toxic form. The interstitial lesions are, however, peculiar to it. There is an absence of the perivascular round-cell infiltration, so prominent a feature in the infective non-suppurative form of encephalitis, but 'productive' changes in the blood-vessels are pronounced. There is proliferation of the adventitia and of the endothelium and formation of new capillaries. The cortex and subcortical white matter, the basal ganglia, cerebellum, mid-brain, cord, choroid plexuses, and meninges all show excessive vascularization, and newly-formed vessels appear more prominently in sections than the normal preformed ones. There is also proliferation of the mesothelial arachnoid cells, and the subarachnoid space may contain large clusters of such cells. Hassin concludes, therefore, that we may speak of infective and of toxic forms of encephalitis, each with its characteristic brain lesion; infiltrative in the former case, and proliferative in the latter. Microscopically, it is possible to determine whether a case of non-suppurative encephalitis is toxic or infective. The arachnoid and subarachnoid space may exhibit changes when the brain tissues proper are normal. F. M. R. W.

Sachs, E., and **Alvis, B. Y. Anatomic and physiologic studies of the eighth nerve.** *Arch. Neurol. & Psychiat.*, 1921, **6**, 119.

This experimental research was carried out on dogs, and the conclusions reached are based upon the study of the symptoms and tract degenerations following section of the vestibular nerve (25 experiments) and destruction of one labyrinth (30 experiments). The *anatomical conclusions* are as follows: (i) No fibres run directly from the semicircular canals to the nuclei of the vestibular nerves. (ii) Very few fibres run forward from Deiter's nucleus, and these do not reach the third or fourth nerve nuclei. (iii) No fibres pass from Deiter's nucleus to the lateral lobes of the cerebellum. There is no anatomical evidence of any connexion between this nucleus and the cerebellum. (iv) Some fibres from Deiter's nucleus end in the posterior corpus quadrigeminum of the same side. (v) All vestibular nerve-fibres end in the vestibular nuclei or in the roof nuclei.

The *physiological conclusions* are that (i) The only constant and essential symptoms of eighth-nerve section or of labyrinth destruction are nystagmus and deviation of the homolateral eye downwards and outwards. (ii) The so-called cerebellar attitude of the head is due to involvement of the middle cerebellar peduncle. (iii) Circus movements, rolling movements, ataxia, swinging, and abnormal attitudes of the head are due to lesions of cerebellar nuclei or peduncles.

These conclusions are only partly in accord with those of Magnus and de Kleijn (1912–13), whose observations were far more extensive and elaborate than those here recorded, and probably, therefore, they will not be accepted in their entirety.

In this connexion it is interesting to note that in their historical review of previous work on the subject, Sachs and Alvis make no mention of the analytical studies of Magnus and his collaborators, though they may be said to have revolutionized our views on the physiology of the vestibular nerve and labyrinth, and are by far the most exact observations on this difficult subject. F. M. R. W.

Garland, J., and **White, P. D. Paralysis of the left recurrent nerve in association with mitral stenosis.** *Arch. Int. Med.*, 1920, **26**, 343. (*Arch. Neurol. & Psychiat.*, 1921, **6**, 351.)

The authors have collected sixty-one cases from the literature. Among the explanations current are pressure atrophy or neuritis from an enlarged left auricle, thrombosis of the left auricle, &c. From the study of nine personally observed cases, the authors conclude that the pulmonary artery exercises some pressure on the nerve, but thrombosis of the left auricle, its dilatation in auricular fibrillation, and chronic mediastinitis may also be contributory causes. Hoarseness, dyspnoea, and cough are the symptoms complained of.

The authors do not specifically refer to the occurrence of this condition as a complication of beri-beri, though the Japanese observers have recorded it both in the infantile and adult forms of this disease, attributing it to the pressure on the nerve of a dilated left auricle. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Cattaneo, D. Sulle cellule giganti da corpi estranei. [**On foreign body giant cells.**] *Arch. per le sc. med.*, 1920, **43**, 202.

Torraca, L. Contributo allo studio delle cellule giganti da corpi estranei per mezzo della colorazione vitale. [**On the formation of foreign body giant cells.**] *Haematologica*, 1920, **1**, 156.

In his experiments Cattaneo had resort to the aseptic introduction into the subcutaneous tissue of fragments of elder-tree pith, small tubes of celloidin, suspensions in physiological solution of Kieselguhr, and fragments of transplantable tumours of the mouse mixed with small quantities of Kieselguhr. The histological study of the inflammatory tissue and aseptic granulomata thus obtained led the author to the following conclusions: (1) The formation of giant cells is connected with the physical and chemical properties of the foreign bodies used for their production. (2) Foreign body giant cells originate at first from the cytoplasmic fusion of 'mononuclear basophil wandering cells', then also from amitotic and mitotic division of their nuclei. (3) Foreign body giant cells remain unaltered for a long time in their site of origin and do not take part in the formation of connective tissue.

Torraca's investigations were carried out on necrotic foci experimentally caused in the liver of rabbits by ligaturing to it, by means of a silk suture, a part of the great omentum. The animals were killed at various intervals after having been intravenously injected with a 1 per cent. solution of lithium carmine sterilized by boiling and filtered through paper. The results obtained were in many points similar to those attained by Cattaneo and may be summarized as follows: (1) In necrotic foci foreign body giant cells originate from typical histiocytes (Aschoff and Kiyono). These conglutinate into syncytial forms within which amitotic as well as mitotic nuclear divisions take place. The giant cells thus produced co-operate in the destruction and reabsorption of the necrotic tissue. (2) Round the silk threads of the suture other giant cells can be seen which do not originate from histiocytes but from cells apparently similar to fibroblasts. These also fuse into large elements within which the original nuclei continue to multiply. (3) In the reabsorbing fragments of adipose tissue giant cells are found which seem to originate through a process of fusion of fat-cells. (4) From a general point of view one may assume that foreign body giant cells can be formed from cells of different kinds. C. d. F.

Gold, E. Über Bronchuscysten und deren Entstehung. [**On cysts of the bronchi and their origin.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 278.

This malformation of the large bronchi appears to be so rare that no specimen of it was found by the author in the Museum of the Pathological Institute of the University of Vienna. However, he was able to collect in a relatively short time four cases, three of which were observed by mere chance at the post-mortem examination of three children, one newly born, one of 3½ months, and one of 3¼ years of age. In the fourth case the existence of the malformation had been suspected when the subject, a little boy of 7 months, was still alive. The malformation is, in the main, characterized by the presence in the posterior mediastinum of one or, more rarely, two cysts of changing dimensions but generally measuring about 3½ × 2·5 × 2·5 cm. The cysts take origin from the bifurcation of the trachea, with which they are in direct continuation. Their internal surface is lined by ciliated epithelium, and their walls, essentially formed of connective tissue, contain remains of a rudimentary lung. C. d. F.

Loeschcke, H. Die Morphologie des normalen und emphysematösen Acinus der Lunge. [**The morphology of normal and emphysematous pulmonary acini.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 213.

The usual histological methods are little suited for the morphological study of pulmonary acini either from the normal or pathological points of view. Particularly in cases of emphysema and bronchiectatic conditions microscopic sections convey only incomplete information as to alterations of the form of pulmonary alveoli, atria, and respiratory bronchioles. The injection methods now and then proposed by various authors are carried out with difficulty and are uncertain in their results. For these reasons the author has thought of filling up the lungs with a metallic mass with subsequent corrosion of the animal matter by means of antiformin. Judging from the pictures which illustrate his paper, in cases of normal and emphysematous lungs, the results are, from a morphological point of view, very instructive. The method can be carried out as follows: the lung, carefully removed from the body with its principal bronchus, is tied by means of this to a running-water blow-pipe and made to expand under the smallest possible pressure. It is then left attached to the pipe until completely dry, viz. until its weight, repeatedly tested by means of a balance, has become constant. To avoid putrefactive alterations, particularly frequent in cases of pathological specimens, a bottle with formalin can be interpolated between blow-pipe and lung. Or the lung, and if possible the whole body, is injected and fixed by means of a solution of formalin before opening the thorax. Once the lung is dry, it is only necessary to gently fill it up from the bronchus with ‘Wood's metal’, which melts at about 80° C. When cold the specimen is subjected to the corrosive action of antiformin. The excessive dilatation of the acini and the thinning of their walls, caused by the previous treatment of blowing and drying, are more than compensated for by the reduction in volume of the solidifying metal so that, in the end, the spaces between the alveolar passages are larger than they ought to be. This defect, however, has no importance when comparing normal and pathological specimens prepared in the same manner, and perhaps renders more instructive the metallic models of normal lungs. C. d. F.

Wätjen. Zur Pathologie der trachealen Schleimdrüsen. [**On the pathology of the mucous glands of the trachea.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 58.

The alterations found in the mucous glands of the windpipe in cases of grippe are not specific, since similar changes can be observed in cases of poisoning with a suffocating gas ('Gelbkreuzgas'), true diphtheria, and small-pox. The alterations are of two kinds, viz. functional and structural. The functional changes are characterized by increased activity, secretory exhaustion, thickening and stagnation of mucus, and presence within the glandular tubules of a qualitatively altered secretion. The structural changes consist of degeneration, desquamation, and necrosis of the glandular epithelium. Between functional and structural changes there is an intimate relation in the sense that the former generally precede the latter. The mucous glands may be locally or diffusely affected; but the structural changes are almost always focal in character. The diffuse affection leads to the 'glandular collapse' characterized by the presence within the glandular tubules of a qualitatively abnormal mucus. The functional changes render possible secondary bacterial invasions of the mucous glands from the superficially affected mucous membrane. The germs thus penetrating into the glands, and sometimes even into their acini, may cause a necrotic disintegration of both the glandular parenchyma and glandular framework, with the subsequent formation of abscesses of the tracheal wall. These, through the existing communications between lymph vessels of the windpipe and of bronchial tubes, may, in their turn, give origin to purulent inflammatory processes of the lungs, mediastinum, pleura, and pericardium. The mechanism of action of the changes in the secretory function of the mucous glands may be somewhat different. Indeed the glandular alteration may at first simply deprive the tracheal mucous membrane of its protective layer of mucus. The thus dried-up mucous membrane, in conjunction with a loss of its ciliated epithelium, such as one can see in cases of grippe, diphtheria, and small-pox, may represent a favourable condition for a further vigorous development of germs and their possible penetration into the pulmonary tissue. This might explain the very rapid formation of pulmonary abscesses which sometimes occurs in cases of grippe and poisoning with 'Gelbkreuzgas'. However, the alterations of mucous glands found in cases of grippe, diphtheria, small-pox, and poisoning with 'Gelbkreuzgas' are not primary bacterial but toxic in character. Experiments made by the author on animals have confirmed this observation and point to a possible analogy between the chemical constitution of the toxins of diphtheria, grippe, and small-pox and that produced by the poisoning with 'Gelbkreuzgas'. Histological investigations have shown that, in spite of an apparent macroscopic similarity, applications to the mucous membrane of the windpipe of concentrated solutions of mineral acids, alkalis and corrosive sublimate, phosgen, vapours of ammonia and osmic acid, do not cause the alterations of the mucous glands characteristic of the form above mentioned. This appears to be due to the fact that caustic agents act directly and not through the medium of a toxin responsible for the described changes as in cases of grippe, diphtheria, small-pox, and poisoning with 'Gelbkreuzgas'.

The varying mode of action and different changes observed in the two groups of altering influences considered by the author have also a practical value in so far as their knowledge can be used for forensic discriminative purposes in the case of inflammatory processes of the windpipe aetiologically obscure. C. d. F.

Boeminghaus, E. Über den Wert der Nilblaumethode für die Darstellung der Fettsubstanzen und den Einfluss einer längeren Formalinfixierung auf den Ausfall der Färbung. [**On the value of the Nile blue method for the demonstration of fatty substances and on the influence of long formalin fixation on the failure of the stain.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 533.

The starting-point of the author's investigations was the observation that in formalin specimens from different cases of fat-embolism of the lungs the fat drops after a time stained no longer red but deep blue by the Nile blue method. A research was consequently planned with the double object of experimentally establishing the cause of such a change, and of testing once more the value of the Nile blue method for the differential staining of fats and fatty acids. For this purpose various pure fatty substances and materials containing much fat were treated according to L. Smith's method (*J. Path. & Bacteriol.*, 1907, **12**, 1), after short and long periods of fixation in formalin solutions, both at room temperature and at that of an incubator at 40°–50° C. The results obtained may be summarized as follows: The statement that Nile blue sulphate stains neutral fats red and fatty acid blue does not hold good in all cases. The affinity of Nile blue sulphate for fatty substances is, from a general point of view, rather small. Pure fatty substances are often stained very faintly or not at all. Of the investigated substances oleic acid and its ester-like compound were found to be the most energetically stainable. Oleic acid stains blue, its ester compounds intensively red, both when tested by themselves or mixed with other fats. The staining manner of fatty substances and their mixtures cannot be relied upon for drawing any sure conclusion as to the presence of this or that fat. An intensive blue tone, however, proves the presence of free oleic acid in the tested mixture or tissue. Neutral fat stains red in tissues fixed in formalin solutions, as long as the formic acid, present in a varying quantity in all of them, particularly when old, has not brought about its splitting into fatty acids and glycerol. C. d. F.

Heijl, C. F. Aus dem Grenzgebiet zwischen Missbildung und Geschwulst. [**From the boundary between malformation and tumour.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 359.

Letterer, E. Über heterotope Geschwülste der Aderhautgeflechte. [**Heterotopic tumours of the choroid plexus.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 370.

Heijl gives an account of his histological investigations on a sacral parasite which from an oncological point of view would be considered as a transitional form between the teratoma and teratoblastoma. Indeed it contained foetal remains of most organs as in teratomata, but mixed in a quite chaotic manner as in teratoblastomata, though without a manifest tendency to autonomous tissue proliferations.

Letterer described four tumours of the choroid plexus, very likely due to a congenital misplacement of tissue rudiments. Of the tumours two were enchondromata, one a glioma, and one a very interesting and rare ganglio-neuroma myelinicum. C. d. F.

Kraus, E. J. Pankreas und Hypophyse. [**Pancreas and pituitary body.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 258.

By means of complete or almost complete extirpation of the pancreas it is possible to cause in cats changes of the pituitary body which do not essentially differ from those observed by the author in the same organ in cases of diabetes mellitus (*Virchow's Arch. f. path. Anat., &c.*, 1920, **228**, 68). Such changes chiefly occur in the anterior lobe of the hypophysis, where an almost complete disappearance of the oxyntic cells can be observed. The surviving ones, which are irregularly distributed throughout the organ, appear smaller than in normal conditions, with a deformed cytoplasm and pycnotic nuclei. At the same time the average weight of the hypophysis is notably diminished. The alterations grow in proportion to the extension of the defect of pancreas, viz. of its islets. Hence the conclusion that the oxyntic cells of the pituitary body take an active part in the metabolism of sugar, and are functionally dependent upon the Langerhans islets.

After the extirpation of the pancreas in cats the pars intermedia and pars nervosa of the pituitary body likewise show changes of an atrophic character. The thyroid gland reacts to the removal of the pancreas, at first with an increased function, as proved by its increase in weight, but after a time it also undergoes a certain degree of atrophy. In the adrenals the lipoids disappear from the cortex, the chromaffinity from the medulla. As to the degenerative organs, an atrophy of the seminiferous tubules and of the interstitial cells of the testicle and ovary were observed in single cases. The pineal body likewise undergoes atrophy. The parathyroid glands appear to be the least affected. C. d. F.

Jaffé, H. Über die extramedulläre Blutbildung bei anämischen Mäusen. [**On the extramedullary formation of blood in anaemic mice.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 224.

It is possible to produce in mice an extramedullary haematopoiesis by means of: (1) chronic intoxications with haemolytic substances; (2) repeated and prolonged blood-letting; (3) grafting of transplantable tumours. The first organ to react in an extensive manner is the spleen, probably owing to the fact that the spleen of normal mice contains a considerable amount of myeloid tissue. In the case of anaemic mice this becomes developed in the spleen pulp, and its production appears to be independent of the Malpighian corpuscles. These, however, behave differently in different forms of anaemia. In those consequent on blood-letting they are larger than normal and show greatly developed germinative centres in which many dividing cells can been seen. When haemolytic poisons are used the Malpighian corpuscles are, on the contrary, greatly diminished in size and may be reduced to simple remains of lymphatic tissue in the neighbourhood of the arteries. This fact appears to be connected with a sort of aggressive tendency of the freshly and strongly developed myeloid tissue. The changes of the spleen after successful grafting of tumours are similar to those consequent to blood-poisoning. The atrophy of the lymphoid tissue of the spleen has a parallel in the diminished number of leucocytes in the circulating blood.

The organs next showing the presence of newly-formed myeloid tissue are the lymph glands, but only after blood-letting, because after poisoning they become greatly atrophied. Nevertheless, if before injecting the animal with poisons such as phenylhydrazin or pyrogallol, the spleen is surgically removed, then the lymph glands greatly increase in size and are almost entirely occupied by myeloid tissue. A similar fact can be observed if blood-letting is carried out after splenectomy. This confirms the view that lymph glands may, in certain conditions, vicariously take over the function of the spleen.

A formation of myeloid tissue in the liver was also seen by the author, particularly after poisoning with phenylhydrazin and pyrogallol, and occasionally after blood-letting. The same fact was much more conspicuous when the animal previously underwent splenectomy. One should add that in consequence of poisoning with the above-mentioned substances a fatty degeneration of the liver-cells and a formation of small foci of necrosis was, now and then, noticed. A production of haematopoietic tissue in other organs, such as, for instance, the cortex of the adrenal, was not observed.

C. d. F.

Löwenthal, K. Zur Pathologie der Zirbeldrüse. Epiphysäre Fettsucht bei geschwulstförmiger Entartung des Organs. [**On the pathology of the pineal body. Obesity due to tumour-like changes of this gland.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 207.

A young man of 23 years of age developed a tumour of the pineal body, the first clinical manifestation of which was a progressive obesity. The other symptoms and signs of increased brain-pressure made their appearance only at a later stage. The tumour was epithelial in structure and similar to the functioning pineal gland of the new-born. This observation supports the view that fatty metabolism can be modified directly through pineal activity, and points to the possible existence of a form of obesity due to hyperpinealism.

C. d. F.

Priesel, A. Ein Beitrag zur Kenntniss des hypophysären Zwergwuchses. [**A contribution to the knowledge of hypophyseal dwarfism.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 220.

The author has had the opportunity of carrying out the post-mortem examination of a dwarf who had reached the remarkable age of 91 years. A bilateral lobular pneumonia had been the immediate cause of his death. Besides a recent cystitis, a moderate degree of arteriosclerosis and senile atrophy of most organs were observed. As to the endocrine glands the following changes were noted: (1) Thyroid and suprarenal glands very small; (2) lateral parathyroid glands uncommonly large (true hyperplasia); (3) genital organs hypoplastic; (4) traces of an old and in part disappeared obesity; (5) important alterations of the pituitary body, the anterior lobe of which was extremely reduced in size, and its glandular parenchyma formed of only a few and incompletely differentiated cells; its posterior lobe was dystopic, viz. situated outside the *sella turcica*; the junction between the two lobes anomalous and incomplete. The author lays stress particularly on this fact, which probably had an injurious influence upon the nutritive conditions of the anterior lobe, and ultimately caused its atrophy, at approximately the age of sexual development. The primary cause of these alterations appear to have been the persistence of the cranio-pharyngeal canal and an anomalous ossification of the posterior half of the sphenoid.

C. d. F.

Mittasch, G. Über Hermaphroditismus. [**On hermaphroditism.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 142.

v. Keussler, H. Über einige Fälle von Hermaphroditismus. [**On some cases of hermaphroditism.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 416.

Poll, H. Zwischenzellengeschwülste des Hodens bei Vogelmischlingen. [**Tumours of the interstitial cells of the testis in bird hybrids.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 40.

Mittasch has had the opportunity of fully investigating a case of 'true' male hermaphroditism. The generative glands had the form and situation of the ovary, but the structure of the testis. Most seminiferous tubules were lined by a stratified germinal epithelium, but no transformation into sperm-cells or fully-formed spermatozoa were seen in any section of the serial preparations. Other tubules showed all degrees of atrophy and degeneration. The interstitial tissue was greatly increased and essentially formed of triangular or polygonal cells provided with large nuclei and rather dense cytoplasm often containing granules of brown pigment and droplets of fat. The accessory system of the male generative gland (rete testis, epididymis, vesicula seminalis, and prostate) was complete and sufficiently well developed. The vas deferens had a somewhat anomalous situation and, while opening in the vesicula seminalis as normally, ended blindly on the side of the epididymis. Of the female generative organs the Fallopian tubes, uterus, and vagina were present and rather well developed. The Fallopian tubes had no abdominal ostia; the uterus was formed as usually of a body and a cervix; this last continued with the rather short vagina which opened into the male urethra at the place where the prostatic utricle and verumontanum are normally situated. Fallopian tubes, uterus, and vagina were filled with coagulated blood, of which some existed also in the vesiculae seminales. The external genitalia and the secondary sexual characteristics were entirely of the male type. However, it appeared from the life-history of this hermaphrodite that he was incapable of sexual intercourse, and that he had been feeble-minded from the age of six. According to Klebs's classification the proper denomination for such a case should be '*Pseudohermaphrodismus masculinus internus*'. The author, however, is of the opinion that both true and pseudohermaphroditism are different manifestations of one and the same primary deviation from the norm, affecting, in changing degrees, the whole generative system.

v. Keussler's paper has the double purpose of proposing a new classification of hermaphroditism and of showing that Steinach's doctrine, of the determining influence of the interstitial gland of the testis ('puberty gland') upon the secondary sexual characteristics, is untenable. For such a purpose three different cases are considered. The first one, previously described by Brühl (*Diss. aus d. path. Inst., Freiburg i. B.*, 1892–4), was a child of 2½ months with female external genitalia, vagina, and uterus of normal form and structure; a cord-like structure, morphologically similar to the Fallopian tube, was shown by Brühl to be without lumen. In the place of ovaries, testicles were found histologically identical with those of a normal child of the same age. No trace of the epididymis and vas deferens was seen in many serial sections. This case is against Steinach's theory, because no pathological change of the interstitial gland was found. According to the new classification it should be termed: *Pseudohermaphroditismus* *anatomicus (P.H.A.) certus masculinus genitalis subsidiarius internus et externus.* The second case was a 20 years old subject considered as a girl in spite of the fact that the body conformation was, on the whole, more that of a boy than that of a girl, and that the beard had started growing two years before. The external genitalia consisted of a small and totally hypospadic penis, so that the urinary meatus might have been mistaken for a short and narrow vulval slit. There were no testicles, and the two halves of the scrotum were so short and flabby as to look like the labia majora. The perinaeum was of the male type. The subject's voice had a peculiar tone intermediate between that of a man and that of a woman. An operation was performed during which the existence was ascertained of a testis with epididymis and of an oviduct with fimbria on the left side, of an oviduct with a body similar to an ovary on the right side. The left 'testis' and right 'ovary' were surgically removed and histologically investigated. It was thus proved that the left generative gland had really the structure of a testis, though without spermatozoa. Its interstitial tissue was richly developed. The right ovary-like body was, as a matter of fact, chiefly formed of interstitial cells, in the main similar to those of the normal ovary, but the apparent follicles passed, through many transitional stages, into canaliculi in every way similar to the tubules of the left testis. In places, the interstitial tissue of this structurally rather undetermined body was so thickly arranged as to recall the picture of an endothelioma. v. Keussler, therefore, admits that this case could not be said to be quite against Steinach's theory, since the interstitial tissue was, at least on the right side, so highly developed and similar to that of the female endocrine gland as to overshadow the fact that on the other side the interstitial gland was of an undoubtedly male aspect, and that the hermaphrodite had external characteristics of a partially female type. According to the new classification this case should be termed *P.H.A. incertus subsidiarius int. et ext.* The third case of v. Keussler appears to be decidedly against Steinach's doctrine. The subject was apparently a 'happily married woman' who went into a women's hospital because of a gonococcal urethritis. The body conformation could have been described as a mixture of male and female anatomical characteristics. The external genitalia were those of the female sex, but the normal vagina ended blindly in a sort of scar tissue. No trace of the uterus and adnexa were found. From both inguinal canals a testis-like body was removed. This was first investigated by Aschoff and then by v. Keussler, and found to be formed of tubules morphologically similar to those of a normal testis, but lined by a non-differentiated epithelium which might have consisted of Sertoli's cells. In places the tubules had a very thin wall and were tightly arranged in nodular masses like adenomata. The interstitial tissue was not exceedingly developed and in every way similar to that of a normal testis. If Steinach's theory of the determining influence of the puberty gland were true, this interstitial tissue ought to have been like that of an ovary. From the point of view of the new classification, this case should be termed '*P.H.A. incertus subsidiarius int. et ext. extragenitalis ext. et psychicus*'.

In connexion with the above observations and discussions, Poll's investigations on the testicles of two hybrids obtained from a peacock and a guinea-hen may be mentioned. The two birds were killed when 4 and 5 years old and termed Nos. 269 and 280. Each of them had two testicles, the left of which was larger than the right, but the left testis of the hybrid No. 280

was larger than that of the same side of the hybrid No. 269. A common characteristic of the four testes was the disappearance and degeneration of the seminiferous tubules, while the interstitial cells had multiplied to such an extent as to form nodules in every way similar to those of an 'alveolar new growth'. The author was not able to decide if these tumours of the interstitial tissue were really malignant in character, as no secondary nodules were found in other organs. However, he points out that the absence of metastases might have been due to the fact that the two hybrids were killed too soon, and that 'disseminated tumours' of the abdominal cavity were observed by Ghigi (*Mem. d. r. Acc. sc. di Bologna*, 1911, **7**, 331) in the only hybrid of the same sort which appears to have been previously, though incompletely, investigated. At any rate, and whatever the degree of malignancy of these tumours might have been, the facts observed point to the existence of an intimate relation between degeneration of a malformed germinative tissue and hyperplasia of the interstitial cells, both phenomena being probably connected with an original defect of zygotes due to the conjugation of heterogeneous gametes. This in the case of hybrids. As, however, similar facts have been described in the ovo-testis of human hermaphrodites, one feels justified in thinking that such deviations from the normal development might likewise be due to an original defect of the gametes or of the product of their fusion. C. d. F.

LEUPOLD, E. Die Bedeutung des Thymus für die Entwicklung der männlichen Keimdrüsen. [**Influence of the thymus on the development of male generative glands.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 472.

The present paper is a continuation of the author's investigations on the relations between suprarenal glands and male generative glands (*Veröffentlichungen a. d. Geb. d. Kriegs-u. Konstitutionspath.*, Fisher, Jena, No. 4, 1920). As a conclusion to his previous and present researches he puts forward the following suggestions: The thymus appears to have a determining influence upon the development of the testes in extra-uterine life in general, and particularly upon its slow but steady growth during childhood and puberty. The size of both thymus and testes is constitutionally determined; these last, however, reach their constitutional dimensions and sexual maturity only during puberty provided that the thymus be unimpaired. But if the normal involution of the thymus is pathologically accelerated, the development of the testes is hindered even during childhood, and they may undergo a more or less marked process of atrophy. The further influence of the thymus on the full maturation of the testes appears to manifest itself through the intermediary of the suprarenal glands. Indeed when these are either hypo- or hyper-plastic, the testes are likewise either smaller or larger than in normal conditions. If the thymus undergoes an involution too early, the suprarenal glands are insufficient *per se* to further the progressive development of the testes or to prevent their atrophy. On the other hand, in cases of persistence and hyperplasy of the thymus, this, provided the adrenals are normally developed, continues to influence the growth of the testes, which may reach uncommon dimensions and a very high degree of histological and functional maturity. However, this cooperation of thymus and adrenals in furthering or hindering the final development of the testes is not quite clear and needs further investigations. C. d. F.

Roth, H. Beitrag zur Kasuistik der Hypophysentumoren. [**A contribution to the casuistics of the tumours of the pituitary body.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 309.

Description of a very large malignant adenoma of the anterior lobe of the pituitary body, observed in a man of 29 years of age. The tumour had had a rapid development and had penetrated into the right lateral brain ventricle. Large secondary nodules were observed in the right occipital and temporal lobes. It appears from the author's investigations that tumours of the pituitary body of such a nature and size are of rather rare occurrence. C. d. F.

Sternberg, C. Über echten Zwergwuchs. [**On true dwarfism.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 275.

After reviewing the actual state of knowledge on the subject the author summarizes the life-history of a case of 'true' dwarfism on which complete histopathological investigations were carried out. The 92 cm. long dwarf was a male of 17 years of age, dead in consequence of an old tuberculous spondylitis. Though the shortness of the body was in part due to the pathological condition of the vertebral column, all other characteristics were those of Hansemann's '*Nanosomia infantilis*'. The body was of a normal size at birth, and his development had also been normal for the first 18 months, when the subject fell from a chair. According to the information obtained from his parents he developed sometime afterwards a very marked gibbosity and became a cripple. He went to school and was very intelligent. With the exception of the chronic tuberculosis of the spine and left femur the post-mortem examination showed the absence of any other pathological process. The limbs were very short and infantile; the bones extremely gracile with permanence of the epiphyseal lines of junction; the genital and internal organs proportionately small. Beard, axillary, and pubic hair were absent. The endocrine glands were likewise exceptionally small but without any special regressive changes. The histological picture of the testicles, to which the author paid special attention, was that of an incomplete development or a true hypoplasia, without any trace of a secondary atrophy as sometimes observed in consequence of various alterations of the pituitary body. As a result of this investigation, and after a careful comparison with similar observations, both of his own and other authors, Sternberg comes to the conclusion that in the present instance the hypoplasia of the endocrine glands and the defective growth were coordinated manifestations of a general defect in the progressive development of the whole organism; in other words, a true case of Hastings Gilford's ateliosis. For this form of dwarfism, not connected with the deficient function or disease of any determined organ, Sternberg proposes the term '*Nanosomia hypoplastica*', reserving that of '*Nanosomia pituitaria*' for the cases due to an essential alteration of the hypophisis cerebri.

In accordance with these denominations Sternberg proposes the term '*Nanosomia thyreogenes* or *hypothyreotica*', to indicate a form of 'true' dwarfism connected with the defective development of the thyroid body. Of this form Sternberg gives the following interesting instance: Dwarf 126 cm. long, dead at the age of 20 of an intercurrent pneumonia. His father had been an alcoholist and died at the age of 43 of tuberculosis.

The boy was of normal size at birth, but had learned to walk only at the age of 6 and to speak at that of 8. At 10 he measured 105 cm. in length, which is approximately the size of a male child of 6 years of age; his intelligence was so little developed that he had to be sent first to a school and then to an asylum for feeble-minded children. In the following 10 years he grew only another 21 cm. in length, but showed no intellectual development, so that he was considered an idiot. The secondary sexual characteristics never developed; the genital organs remained very small. At the post-mortem examination Sternberg found that the trunk and limbs were short but proportionate; the bones were gracile and of an infantile type. The internal organs and endocrine glands were likewise proportionately small. The histological investigation of the testicles showed that they had, at least up to a point, developed normally, and had then undergone a secondary atrophy characterized by a remarkable thickening and hyaline degeneration of the walls of the seminiferous tubules, many of which were completely obliterated. No changes were found in the endocrine glands with the exception of the thyroid body, the most conspicuous alteration of which was the almost complete absence of colloid. In addition, the vesicles of one of its lobes were lined by a high cylindrical epithelium, and were structurally similar to those of the thyroids of the new-born; only a few vesicles of the other lobe showed such a picture, most of them being filled with cubical epithelial cells.

This observation appears to justify the proposed separation from the *Nanosomia hypoplastica* and *pituitaria* of a *Nanosomia thyreogenes*, clinically characterized by defective though proportionate development of the whole organism, very slow but still steady body growth, partial permanence of the epiphyseal lines of junction, and chiefly by intellectual deficiency. It could be differentiated from the cretinic form of dwarfism because of the characteristic want of proportion of the latter. C. d. F.

Amantea, G., e Krzyszkowsky, C. Sulla cristallizzazione dell' emoglobina. [**The crystallization of haemoglobin.**] *Arch. d. Fisiol.*, 1920, **18**, 87.

Numerous different methods have been suggested from time to time by various investigators for the purpose of obtaining the crystallization of haemoglobin. Many of them, however, are applicable only to the blood of one or two animals, or not suitable for class and demonstration purposes. A research was therefore commenced by the authors with the object of finding, if possible, some method which would answer in almost every instance. The results obtained are: To prepare crystals of haemoglobin in a quick and sure way the blood of *Vespertilio nettereri* appears more suitable than that of any other animal. At the time of hibernation crystals can be obtained by simply putting a drop of its blood on a slide under a cover-slip and letting it stand for a little while. The blood of other species of bats is not so suitable for the purpose. The most general method for obtaining crystals of haemoglobin appears to be the direct treatment on a slide of blood with a small quantity of powdered saponin. In the case of animals with nucleated erythrocytes one should preferably have resort to the direct treatment of a drop of blood either with a small quantity of powdered gum arabic or with a drop of a mixture consisting of 1 c.cm. of saturated watery solution of saponin, one drop of 10 per cent. ammonia, and half a c.cm. of ether. By the saponin method the crystallization of haemoglobin can be obtained from guinea-pigs' blood almost as quickly and easily as from that of *V. nettereri* at the time of hibernation. As pointed out by Monckton Copeman (*J. Physiol.*, 1890, **11**, 401), it is extremely difficult, if not impossible, to obtain crystals of haemoglobin from fresh blood of normal human subjects.

It might be added that the old method of Gamgee, as recommended by Halliburton and Monckton Copeman, is for class purposes perhaps the most suitable of all. To the defibrinated blood of a guinea-pig one-sixteenth of its volume of ether is added; after some vigorous shaking the fluid is set aside in a cool place for 24–48 hours, when crystals will have formed in a quantity sufficient for distribution to a large class of about 100 students.

C. d. F.

Patania, G. Influenza dell' alcool sulla funzione del cuore. [**Influence of alcohol on the function of the heart.**] *Arch. di Fisiol.*, 1920, **18**, 67.

The present research was undertaken because no definite conclusions appear to have as yet been reached in regard to the action of alcohol on the function of the heart. Some authors hold that it chiefly increases the cardiac activity; others again are of the opinion that its action is essentially depressive; and yet others think that very small doses act in an exciting manner while large ones have an opposite effect. Moreover, no one seems to have studied the action of alcohol on the excitability of the myocardium, to which the author has paid particular attention. In addition, he has investigated the effect of the excitation of the vagus and the contraction curve of the frog's heart. This was exposed and suspended to a lever according to Engelmann's method. After taking a normal tracing, varying quantities of ethyl alcohol diluted with Ringer's solution were injected into the frogs and other tracings taken at intervals of from 5 to 20 minutes. The results obtained, which are of general interest, have been summarized by the author approximately as follows: (1) Ethyl alcohol noticeably modifies the activity and functional properties of the heart. (2) This action manifests itself in a slackening of the heart's rhythm, which is chiefly due to a remarkable prolongation of the systolic phase when small doses are used, to a prolongation of the diastolic phase in the case of large ones. (3) The excitability of the myocardium is constantly increased by small doses of alcohol, but this fact is less and less apparent as the doses become larger, until excitability may even be diminished, with a correspondent elevation of its threshold. (4) The period of latency is constantly shortened by minimal doses of alcohol; somewhat larger ones do not appear to have always the same effect. (5) The length of the refractory period does not show any perceptible modification in the experimental conditions adopted by the author. (6) The excitability threshold of the vagus is increased by alcohol. (7) Under the influence of alcohol the heart stopped by means of a proper stimulation of the vagus re-starts its automatic activity more slowly than in normal conditions. (8) After stimulation of the vagus it takes a longer time for the automatic rhythm to become normal when alcohol is introduced into the organism than in the case of the same heart before undergoing intoxication.

C. d. F.

Azzi, A. Ricerche sul bilancio energetico della rana in condizioni patologiche. [**On the energy metabolism of the frog in morbid conditions.**] *Arch. di Fisiol.*, 1920, **18**, 49.

The total energy exchanges of normal frogs remain fairly constant if the animals are regularly fed and kept in uniform surroundings. After the inoculation of germs pathogenic for cold-blooded animals, frogs may fall ill and die. In this case the energy metabolism may noticeably vary, but in different ways. Sometimes it increases up to a maximum, when it gradually diminishes until death supervenes; sometimes the increase persists and a diminution appears only for a brief moment during agony; in other cases still, no increase can be observed, but a state of collapse characterized by a progressive decline of energy exchanges. The production of heat and consumption of oxygen vary in the same way, though their curves are not quite parallel. After injections of solutions of peptone frogs appear ill for a certain time during which a remarkable increase in the total energy exchanges can be noticed. It results from this that in cold-blooded animals intoxication with bacterio-proteins or derivatives of proteins, generally considered as the principal cause of fever, alters the thermogenesis, sometimes in a positive, sometimes in a negative sense, and sometimes remains without any apparent effect. Hyperpyrexia cannot be adduced to explain this because it is non-existent in cold-blooded animals. It is true that the author (*Pubblic. Staz. Zool. di Napoli*, 1917, **2**, 77) has himself observed in diseased cold-blooded animals changes in the mechanism of production and dispersion of heat resulting in the body temperature exceeding that of their surroundings beyond the normal limit; but the differences are very small (hundredths of a degree centigrade) and practically insignificant. It appears, therefore, probable that morbid agents act on thermogenetic nervous centres sometimes in an exciting, sometimes in a paralysing manner. Hence the observation of quite opposite effects according to the agent employed and to a certain individual mode of reaction which should not be overlooked. The present research also shows that there is a great analogy between the alterations of the energy metabolism during acute infective processes in cold- and warm-blooded animals, and that hyperpyrexia is not a necessary factor of hyperthermogenesis, the increased body temperature and increased heat production being probably governed by different mechanisms and explicable independently one of the other. C. d. F.

Feitis, H. Über multiple Nekrosen in der Milz (Fleckmilz). [**On multiple necrosis of the spleen (speck spleen).**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 297.

The spleen of two subjects, dead in consequence of chronic interstitial nephritis with hypertonia, uraemia, and terminal heart failure, was found occupied by a great number of small and irregularly arranged necrotic masses. In the first case, a man of 39 years of age, the lesion was uniformly diffused over the whole organ; in the second, a gouty man of 60 years of age, the subcapsular portions were most affected. The term ‘speck spleen’ is proposed for such a lesion, which does not appear to have been, as yet, described. A small number of the necrotic foci in the first case and a relatively larger one in the second were histopathologically similar to ordinary infarcts. In both cases the smallest foci had a diameter of about 1 mm., the largest of about 1 cm.; between the former and the latter middle-sized ones could be seen. These, as well as the large ones, appeared to be due to a process of fusion of the small foci. The shape of the foci was quite irregular, the delimitation from the non-affected tissue similar to that characteristic of ordinary infarcts; however, minute initial points of necrosis did not show any definite delimitation of the sort.

In both cases the intima of the small and middle-sized arteries showed a remarkable degree of hyaline degeneration which grew in intensity as they diminished in size, reaching a maximum in the pencils of capillary vessels which open into the interstices of the spleen pulp. In the follicular and trabecular arteries a marked thickening of the adventitia was also noticeable. The lumen of all arteries and capillaries was greatly reduced. The veins and non-necrotic areas of the parenchyma showed the lesions characteristic of chronic venous congestion.

The mechanism of production of the necrotic foci can be found in the alteration of the small arteries and capillaries, as well as in their mode of distribution to the spleen pulp and Malpighian corpuscles. Indeed the total or even partial occlusion of such capillaries appears to be a cause sufficient to determine the pathological picture observed by the author. The reason for its very infrequent occurrence is due to the fact that the spleen is, as a rule, so richly provided with blood-vessels that the consequences of a local, even if very diffuse, ischaemia, is easily counteracted. In concluding considerations the author suggests that the speck spleen should be considered as a further stage of the 'hyaline degeneration of the small arteries of the spleen' described by Herxheimer in diseases clinically characterized by an increased blood-pressure. C. d. F.

Frank, A. Die Genese des Amyloids. [**On the genesis of amyloid.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 181.

The results of his very interesting observations and experiments are summarized by the author nearly as follows: (1) From a pathogenetic point of view, amyloid must be considered as produced under the direct influence of bacteria. (2) The strains capable of such an effect are either little virulent or non-virulent and capable of producing acid and mucus in culture media. (3) In experimental conditions failures in obtaining a production of amyloid are due to the amount of bacteria injected. (4) The property of causing a production of amyloid is not peculiar to certain strains or groups of bacteria, but it is equally possessed by quite different germs, whether alive or dead. However, since such an effect is obtained with greater constancy and intensity by means of living germs than by means of dead ones, the suggestion is made of considering the production of amyloid more as a bacterial intoxication than as an infection in the strict sense generally attributed to this term. (5) The power of producing amyloid probably belongs not to specific toxins of bacteric origin but to proteins and similar materials originating from the disruption of the bacteria, either in the places where amyloid is formed, or in the circulating body fluids. (6) Since amyloid degeneration is more easily obtainable by means of living germs, one may assume that their acid-producing property also plays an important part in the causation of the phenomenon. The frequency of amyloid degeneration in constitutional diseases in the course of which chronic suppurative processes occur, is explained by the fact that in such cases the conditions exist for a continuous penetration into the blood-stream and lymph paths of bacteria and products of their disruption. (7) In experimental conditions the production of amyloid in given organs depends, in general, upon the place chosen for injecting bacteria. As these, however, easily collect in the spleen, one understands why this organ is most and often almost exclusively affected. (8) The specific reactions for the demonstration of the amyloid are probably connected either with the mucus-producing property of the bacteria under the influence of which amyloid is produced, or with the nature of their body substances. (9) From a morphogenetic point of view amyloid can be considered as due to a process of protoplasmic coagulation accompanied by a swelling up of the cytoplasm first of the cells of the walls of blood-vessels and then of other tissue elements. Coagulation and swelling are probably favoured by the acid-producing property of the bacteria which cause the production of amyloid. (10) The amyloid obtained in experimental conditions may either give its well-known reactions from the beginning or be preceded by an 'achromatic stage', this difference being due to the kind of bacteria used for the experiments. C. d. F.

Leischner, F. Über kongenitale Stenose und Achsendrehung des Dünndarmes. [**Congenital stenosis and torsion of the small intestine.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 28.

Crescenzi, G. Di una rara malformatione del tenue. [**Rare malformation of the small intestine.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 1.

In a normally built girl of 13 years of age Crescenzi has observed a malformation of the small intestine characterized by the presence of two diverticula. One, about 5 cm. long, was situated at 43 cm. from Bauhin's valve and was easily identified as a Meckel's diverticulum. The other was situated at 68 cm. from the same valve and measured, in an extended state, 51 cm. It had become developed in the thickness of the mesentery and its mucous membrane had a structure similar to that of the normal stomach. In spite of this fact the author, after considering the mode of development of the small intestine, comes to the conclusion that the second diverticulum was also a malformation of the Meckel type. The interest of Crescenzi's communication lies in the fact that only one other similar case has been described by Roth (*Virchow's Arch. f. path. Anat.* 1881, **86**, 371).

The case described by Leischner is morphologically of a quite different kind but likewise connected with the mode of development of the small intestine. Indeed, at an early period of embryonic life, the small intestine is impervious and only at a later stage becomes hollowed out. During such a process diverticuli may form or points of stenosis residuate. Leischner's case belongs to this second category of malformations. It was observed in a child of 5 days at 45 cm. from the ileo-caecal valve, and was complicated by a complete torsion of an intestinal loop over the point of stenosis. This complication had at first given the impression that the stenosis was secondary to a congenital torsion of a loop of the small intestine, but the author puts forward well-reasoned evidence to the contrary. C. d. F.

Cicconardi, G. Sulle alterazioni istologiche del rene prodotte dal raffreddamento. [**On the alterations caused in the kidney by cold.**] *Arch. per le sc. med.*, 1920, **43**, 247.

Experiments were made on rabbits by means of local and general refrigeration. In the first case either mixtures of ice and salt were applied on the left renal region, or ice was put directly on the exposed kidney. In the second instance the animals were plunged into cold water (of 9° to 12° C.) and kept therein until their body temperature had been lowered by 12° to 14° C. The histological investigation of the kidneys showed that after the application of cold on one kidney the other is almost equally affected, and that general refrigeration is more injurious than local applications of cold. The changes consisted, functionally, of a notable degree of albuminuria with granular casts in the urinary sediment; histologically of haemorrhagic infiltrations of the parenchyma of the kidneys with degeneration and loss of the epithelium of the uriniferous tubules. The same epithelium showed an altered staining power when tested by the carmine intra-vitam method. These changes were plainly visible within the first 24 hours from the beginning of the experiments; in the subsequent days they gradually diminished in intensity, giving place, at about the end of the second week, to a complete *restitutio ad integrum.* The author draws from these results the conclusions that the alterations of the kidney, due to local or general chilling, are primarily of a vasomotor kind; that the kidney is more resistant to the action of cold than was supposed; and lastly that, at least in rabbits, refrigeration either of a local or of general character, is *per se* insufficient to cause a true nephritis. C. d. F.

Pizzetti, D. Contributo allo studio della cosidetta 'pielite granulosa'. [**On the so-called 'pyelitis granulosa'.**] *Arch. per le sc. med.*, 1920, **43**, 182.

The term '*pyelitis granulosa*' (granular pyelitis) has been used to indicate a rare affection of the renal pelvis characterized by the presence in the corium of rather large lymphatic nodules similar to the solitary lymph nodules of the small intestine. The follicles are arranged in rows, and being situated almost immediately under the epithelium they irregularly raise the mucous membrane, which thus acquires a peculiar granular aspect. Some of the follicles may extend upward through the epithelium and give origin to small ulcerations of the renal pelvis. The follicles, which may reach a maximum diameter of even 2 mm., are structurally identical with ordinary lymph nodules, and like these consist of a peripheral dark zone closely packed with small lymphocytes and of a central lighter germ-centre where larger mononuclear leucocytes and many dividing cells are seen. Smaller lymphatic follicles and simple accumulations of lymphocytes are found here and there, and within the corium of the initial portion of the ureter. The principal alteration of the kidney itself consists of a small-celled infiltration chiefly formed of small lymphocytes, which accumulate particularly in the cortex round small blood-vessels, and within and without the Malpighian glomeruli. These often show signs of hyaline degeneration and atrophy. Minute haemorrhages and a proliferation of the interstitial connective tissue also occur. In the affected areas the epithelium of the renal tubules in general, but particularly that of the convoluted tubules, frequently undergo a relatively slight degeneration, while the blood-vessels show endo- and peri-arteritic changes. The affection appears to be monolateral, and is clinically characterized by an accessory haematuria. Nothing definite is known in regard to its pathogenesis. The cases published in addition to the present observation number eight, and are known by the names of the authors who describe them: *Case* 1, Solieri and Zanellini (*Clin. chir.*, 1905, **13**, 97); *Case* 2, Taddei (*Ann. d. mal. d. org. génito-urin.*, 1907, **25**, 55); *Cases* 3, 4, and 5, v. Frisch (*Ztschr. f. Urol.*, 1909, Beiheft **2**, 273); *Case* 6, Baetzner (*Ztschr. f. urol. Chir.*, 1913, **1**, 285); *Case* 7, Bretschmer (*Am. J. Urol.*, 1914, **10**, 113); *Case* 8, Finzi (*Policlin., Sez. Chir.*, 1915, **22**, 509). C. d. F.

Christeller, E. Über agonale Blutungen im Gebiete der oberen Hohlvene. [**On agonal haemorrhages in the domain of the superior vena cava.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 505.

'Agonal haemorrhages' were observed in the connective tissue surrounding the organs of the neck and the arch of the aorta in 78 out of 173 different cases, viz. in 45 per cent. of all cases examined. The 'agonal haemorrhages' appear to be limited to the domain of the superior vena cava, and differ from all those observed *post mortem* up to the present, i. e. from the traumatic, septic, and constitutional (diathetic) haemorrhages, from Tardieu's suffocation haemorrhages, and from Kratter's mediastinal blood-spots. The 'agonal haemorrhages' of the neck are, on the contrary, similar to those visible in the same region in cases of compression of the thorax. With these last they have in common a fundamentally identical cause which might be defined as a congestion from increased pressure in the right half of the heart and in the superior vena cava. There is only this difference, that in cases of compression of the thorax the increased pressure is due to agents acting from outward inward, while in the case of 'agonal haemorrhages' the increased pressure is caused internally by a sudden heart failure. It is worth noting that the last-named haemorrhages manifest themselves very quickly, as the author was able to establish both clinically and anatomically in a certain number of cases. The pathological diagnostic importance of the 'agonal haemorrhages' consists in the fact that they enable one to state, with a very great degree of probability, that death took place through sudden heart failure. C. d. F.

Lepehne, G. Über Fragmentation der roten Blutkörper. [**On the fragmentation of red blood corpuscles.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 352.

The starting-point of the author's investigations was the well-known occurrence of a fragmentation of red blood corpuscles within the cells of the 'reticulo-endothelial apparatus' in general, but chiefly of the spleen in cases of infectious and septic jaundice, icterus neonatorum, typhoïd and paratyphoid fever. He has now observed a similar fragmentation within the glomeruli of the kidney in two cases of chronic interstitial nephritis, and within the blood-vessels in a case of endarteritis obliterans, as well as within the heart and renal capillaries of some fatal cases of diphtheria and tetanus. The author was not able to decide whether such a reduction of red blood corpuscles into minute haemoglobinic spherules and fragments happens *intra vitam* or *post mortem*; however, he points out that it does not occur in all diseases, that it is not due to the action of fixing agents and other treatments of the material, and that it appears not to have been as yet observed within blood capillaries. C. d. F.

STAEMMLER, M. Ein Beitrag zur Lehre von der Cystenniere. [**On cystic kidney.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 22.

After describing and discussing at great length his histo-pathological investigations, the author comes to the conclusion that the cystic kidney of both the new-born and the adult is due to the combination of a congenital arrest of development with a true new growth, viz. a primary multilocular cystadenoma. C. d. F.

BECKER, V. Besteht ein ätiologischer Zusammenhang zwischen Oxyuren und der akuten Wurmfortsatzentzündung? [**Is there any aetiological connexion between *Oxyuris vermicularis* and acute appendicitis?**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 171.

Oxyuris vermicularis is found in 50 per cent. of all normal vermiform processes surgically removed. It gives origin to a symptomatological complex which may be mistaken for a severe attack of acute appendicitis. As proposed by Aschoff, such a malady can be appropriately termed 'appendicopathia oxyurica'. This chiefly affects the female sex, and only in a few cases leads to an alteration characterized by a catarrh of the mucous membrane associated with an inflammatory fullness of the lymph vessels. In appendices surgically removed in consequence of acute appendicitis, *Oxyuris* is found in the same proportions as in those obtained at the P.M. table. An aetiological connexion between *Oxyuris* and acute appendicitis must be excluded. C. d. F.

ASCHOFF, L. Zur Begriffsbestimmung der Entzündung. [**The concept of inflammation.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 1.

If it be admitted that the idea of response to injury or defence is valid for all living organisms, then it follows that: (1) Inflammation can be defined neither according to its manifestations nor according to its nature or significance for the organism. (2) Commonly used definitions based upon clinical and morphological manifestations need amplification in a physiological sense. (3) It will be of no advantage to ascertain the clinical, morphological, and physiological symptomatology of inflammation without ascertaining its biological significance. (4) This consists in the possibility of proving the existence of a state of excitement or reaction of determined intensity on the part of the organism affected. (5) This proof alone would, however, be inadequate, and the symptomatological definition of the reaction must be linked and completed with a functional definition. (6) From a biological point of view we therefore call inflammation the whole of the complex adjustments of the organisms to pathological stimuli, which can be ascertained by means of clinical, morphological, and physiological methods. (7) We distinguish such adjustments by means of the suffix 'itis', and, according to the consequent changes or resulting reactions, we subdivide them into restorative, reparative, and defensive. One should, however, be aware that, on the part of the clinicians, only the defensive forms are considered as inflammatory. (8) We distinguish a general and a local defensive reaction or defensive inflammation. The former includes fever, leucocytosis, the production of antibodies, &c.; the latter comprises the reactive processes manifesting themselves locally in parenchymas, circulatory system, and sustaining tissue. (9) According to the predominating participation of one or the other of these systems, one can speak of parenchymatous, vascular, and interstitial defensive inflammations. The vascular defensive reaction may be further subdivided into exudative, migratory, and diapedetic forms. (10) Parenchyma, sustaining tissue, and circulatory system are affected in changing proportions also in the restorative and reparatory forms of inflammation, so that in special cases we can even speak of 'parenchymatous (reparatory) inflammatory forms'; for instance, in conjunction with severe changes of the parenchyma of the kidney, we would say 'reparatory parenchymatous nephritis'. C. d. F.

Conti, L. Modificazioni ematologiche ed urologiche in una particolare forma di emoglobinuria sperimentale. [**Haematological and urological changes during experimental haemoglobinuria.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 147.

The present research confirms and amplifies Gasbarrini's investigations to which reference has been already made (*Medical Science*, 1921, **3**, 559). In Conti's experiments haemoglobinuric exacerbations were caused in dogs by means of intraperitoneal injections of 5 c.cm. of the laked and isotonized sediment of a centrifuged suspension in physiological solution of the red blood corpuscles of the same animals. The results obtained are: (1) During the haemoglobinuric access the urine contains albumin, oxyhaemoglobin, biliary pigments, and urobilin; the blood shows a diminution of the haemoglobin content and of the erythrocytes, an increase in the total number of leucocytes. These changes disappear a little while after the exacerbation is over. (2) The injections, if repeated at long intervals, prevent the access and cause an increase of the haemoglobin content and of the red and white blood corpuscles. (3) The haemoglobinuric exacerbation can be prevented either by warming the laked and isotonized erythrocytes for three hours at 56° C., or by making an intravenous injection of serum of a haemoglobinuric dog. C. d. F.

Schmincke, A. Über lymphoepitheliale Geschwülste. [**On lympho-epithelial new growths.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 161.

The present paper was written with the purpose of drawing attention to a group of tumours histologically characterized by an intimate connexion between multiplying epithelial cells and lymphocytes. Such tumours occur in the neighbourhood of the palatine tonsils, soft palate, and epipharynx, where they form often ulcerated nodules growing within the oral and pharyngeal cavities. In spite of their size and strong proliferative and infiltrative character, they are clinically held to be relatively benign, in so far as they undergo rapid retrocession up to complete disappearance after treatment with Röntgen and radium rays. Histogenetically they must be considered as 'branchiogenous ectodermal new growths'. They are not rare and are well known to histo-pathologists and laryngologists, by whom they appear to be regarded as sarcomata. Quite recently Schmincke has had the opportunity of collecting five of such tumours. Of these he gives a detailed description, from which it results that they are essentially formed of large cells undoubtedly epithelial in character and rapidly multiplying into a reticulo-syncytial ground substance, thickly infiltrated by lymphocytes. The reason for such an intimate mixture of histogenetically different elements can be found in the normal structure and mode of origin of organs such as the tonsils and thymus. And as for these the denomination 'lympho-epithelial' has been rightly used first by Jolly (*Compt. rend. Ass. anatomistes,* 1911, **13**, 164) and then by Mollier (*Sitzungsber. d. Gesellsch. f. Morph. u. Physiol., München,* 1913, **29**, 14), it appears desirable that the same term should be employed for the tumours derived from the abovementioned or similar formations. In doing so one would implicitly take into due account the results of the investigations of Jolly and Mollier as well as of Maximow (*Arch. f. mikr. Anat.,* 1909, **74**, 525), Hammar (*Ergebn. d. Anat. u. Entwicklungsgesch.,* 1910, **19**, 1), and Hartmann (*Anat. Anz.,* 1914–15, **47**, 65), with the advantage of appropriately defining a group of tumours which, though epithelial in character, entirely differ from the ordinary carcinomata of the mouth and pharynx. C. d. F.

Terni, T. Sull' ipertrofia delle cellule dei gangli spinali che innervano la coda rigenerata della 'Lacerta muralis'. **[On the hypertrophy of the spinal ganglion cells innervating the regenerated tail of *Lacerta muralis.*]** *Giorn. d. r. Acc. med. di Torino,* 1920, **83**, 131.

The present paper is a continuation of a research begun by the author a few years ago, on the relation between the size of spinal ganglion cells and extension of the territory innervated by their peripheral nerve-processes. His first investigations (*Anat. Anz.,* 1914, **47**, 369) were made on the spinal ganglia of various specimens of chelonia (*Thalassochelys caretta, Testudo graeca, Emys europea, Testudo nemoralis*) and led to the conclusion that in normal conditions the size of spinal ganglion cells is in relation to the length and number of collateral ramifications of their peripheral nerve-processes. In a second paper on the subject (*Arch. ital. di Anat. e di Embryol.,* 1919, **17**, 507) the author took into consideration the changes seen in the spinal ganglia innervating the regenerated tail of *Gongylus ocellatus,* and in the present one those observed in the ganglia innervating the regenerated tail of the lizard. In both cases the author looked for a confirmation of the observations made in normal reptiles, and reached conclusions which may be summarized as follows: The regenerated tail of reptiles is similar to that of normal specimens only as regards the external aspect and the reproduction of a musculature of the segmental type. The spinal cord and vertebrae do not regenerate. The motor and sensory innervation of the new tail is supplied by the regenerated fibres of some of the nerves of the surviving tail's stump. In the opinion of Davenport Hooker (*Arch. f. mikr. Anat.,* 1912, **80**, 217) these are, in the case of *Lacerta agilis,* the last two distal pairs. According to Terni, in the case of *Gongylus ocellatus* and *Lacerta muralis,* the surviving and regenerating pairs are the last three. While normally the spinal ganglion cells of the tail of the investigated reptilia are, on the average, smaller than those of the trunk, those belonging to the regenerating nerves are considerably larger and their diameters may even reach dimensions five times greater than those of the corresponding normal cells. The hypertrophic nerve-cells are sometimes found to be larger than the largest ones of the cervical ganglia, which in normal specimens are the biggest of all spinal ganglion cells. This increase in size is the more noticeable the longer is the interval between injury and investigation; or, in other words, the longer is the piece of regenerated tail.

According to Terni this very considerable degree of hypertrophy is due to the fact that each of the regenerating peripheral processes of the affected spinal ganglion cells must provide to the motor and sensory innervation of a portion of the body certainly much larger than that to which they are normally distributed. For this reason, and in view of the results obtained in his previous investigations, he defines the determining factors of the described hypertrophy as 'exceptional morphogenetic stimuli'. These, he thinks, should be considered as different from the 'reactive phenomena' described by van Gehuchten, Lugaro, Marinesco, Da Fano, and other authors in mammals after the section of a cranial or peripheral nerve. It might, however, be pointed out that the difference is more apparent than substantial. As shown particularly by Da Fano (*Beitr. z. path. Anat. u. z. allg. Path.*, 1908, **44**, 495), the hypertrophy of the nerve-cells of a motor nucleus consequent on the section of its corresponding nerve, is not a reactive phenomenon due to the injury itself, but the morphological manifestation of an effort made by the surviving nerve-cells to rebuild the destroyed nerve-path. Indeed it lasts long enough for the complete regeneration of the divided nerve-fibres to take place. In the case of the regenerated tail of reptiles, the hypertrophy of the affected nerve-cells is very remarkable and of a permanent character, because the innervated territory is likewise permanently larger than normally, but the phenomenon seems essentially the same and intelligible without assuming the existence of 'exceptional morphogenetic stimuli'. C. d. F.

KRUKENBERG, E. Beiträge zur Frage des Aneurysma dissecans. [**On dissecting aneurysm.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **67**, 329.

Investigations were carried out on a case of dissecting aneurysm of the aorta complicated by multiple and likewise dissecting aneurysms of both inferior thyroid arteries. The results obtained, and a careful study of the literature on the subject, led the author to the following conclusions: (1) Next to the well-known form of dissecting aneurysm, another one should be considered which draws its blood from the *vasa vasorum* of the arterial walls and again resolves into small fissures and *vasa vasorum*. (2) Both the common and newly-described kinds of aneurysms are due to a 'dissecting arteritis' (Babès u. Minorescu, *Beitr. z. path. Anat. u. z. allg. Path.*, 1910, **48**, 221), and are probably caused by a syphilitic mesarteritis. Mechanical causes, such as an increased blood-pressure, injuries, &c., also play perhaps a part in their causation. (3) Between the two kinds of aneurysms there is perhaps only a difference of degree, so many are the transitional varieties presented by their multiform appearances. (4) A cleft uniting the aneurysmal sac with the lumen of the affected blood-vessels need not exist in aneurysms derived from the *vasa vasorum*. When such is the case, it should not be regarded as a causal factor, but as a consequence of the fortuitous meeting of the dilating sac of a dissecting aneurysm with a profoundly altered portion of the internal wall of the blood-vessel. (5) The same might be said of the so-called 'retrograde inward perforation' in cases of Laennec's dissecting aneurysm. The alteration of the wall of the blood-vessel may be due to the softening of atheromatous foci, fibrous arteritis, &c. (6) However, a uniting cleft may, in the newly-described kind of dissecting aneurysm, be considered as a factor favouring the further expansion of the primary aneurysmal fissure. (7) The so-called young or new intima forming within the ruptured walls of blood-vessels affected by dissecting aneurysms probably originates from the connective tissue surrounding the points of rupture. C. d. F.

BIOCHEMISTRY

Harden, A., and **Robison, R. The antiscorbutic properties of concentrated fruit juices. Part IV.** *Bio-Chem. J.*, 1921, **15**, 521.

The antiscorbutic properties of a dried orange juice which had been kept for 14 months at a uniform temperature of 29° C. was tested. A certain measure of protection against scurvy was afforded, but more than 85 per cent. of its antiscorbutic property was destroyed by keeping at this high temperature. C. G. L. W.

Stammer, A. D. Feeding experiments in connexion with vitamin A and B. (1) The value of steam-distilled palm-kernel oil as a control fat. (2) Wheat bran as a source of vitamins A and B. *Bio-Chem. J.*, 1921, **15**, 489.

Bran undoubtedly contains vitamin A. With steam-distilled palm-kernel oil and bran growth is allowed which is little inferior to that with butter fat. Bran seems to contain sufficient antineuritic properties.

By steam-distilling palm-kernel oil at 230°–260° for 3–4 hours this substance may be made practically free from vitamin A.

C. G. L. W.

Coward, K. H., and **Drummond, J. C. The formation of vitamin A in living plant tissues.** *Bio-Chem. J.*, 1921, **15**, 530.

It is usually assumed that the fat-soluble vitamin occurs in the green, actively assimilating parts of plant tissue and that it is absent from the localities where chlorophyll is not found.

The authors discuss the results which are available on the vitamin content of seeds, of germinating seeds, of etiolated seedlings and green seedlings. They have made experiments with various vegetable tissues, and with the unsaponifiable matter in these tissues. They find that dried seeds generally are deficient in vitamin A, and the amount is not increased by germination. Green leaves form large amounts of the substance. It does not appear to be associated with the proteins, and appears in that fraction of the fat extracted from these which is resistant to saponification.

C. G. L. W.

Drummond, J. C., Coward, K. H., and **Watson, A. F. Researches on vitamin A. VII. Notes on the factors influencing the value of milk and butter as sources of vitamin A.** *Bio-Chem. J.*, 1921, **15**, 540.

The diet of the cow is undoubtedly the chief cause of variations in the amount of vitamin A in milk. Season, apart from the consequent diet, and breed are not the cause of any marked variation. Colostrum is richer in vitamin than later milk. Butter is less potent than milk. Butter shows wide variations as a source of the compound. Most of this is due to differences in the diet of the cow. Tinned butter does not lose its vitamin, only those processes which expose the food to air are destructive.

C. G. L. W.

Pappenheimer, A. M., McCann, G. F., Zucker, T. F., and **Hess, A. F. The effect of various modifications of a diet producing rickets in rats.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 267.

One of the authors with H. C. Sherman has shown that rats regularly develop rickets when fed on a diet consisting of patent flour, calcium lactate, sodium chloride, and ferric citrate. It was further shown that the substitution of 0·4 per cent. basic potassium phosphate for an equal percentage of calcium lactate uniformly protected against the development of rickets. The protection is due to the phosphate moiety of the salt—not the potassium. The use of a yeast vitamin was successful in preventing rickets, but the phosphorus content of this preparation was high. The results with casein were inconclusive, although this preparation contains a quantity of phosphorus sufficient to protect from rickets.

C. G. L. W.

Hess, A. F., McCann, G. F., and **Pappenheimer, A. M. The failure of rats to develop rickets on a diet deficient in vitamin A.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 266.

Rats were placed on a diet deficient in vitamin A. They did not grow, developed eye lesion, and developed many infections. No rachitic symptoms appeared. There was merely an inactive osteogenesis. The authors conclude that a lack of fat-soluble vitamin in a diet otherwise complete does not lead to rickets. C. G. L. W.

Hess, A. F., and **Unger, L. J. The cure of infantile rickets by artificial light and sunlight.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 298.

Cures of cases of infantile rickets are reported by the use of exposures of the entire infantile body to the rays of a mercury vapour lamp at a distance of 120–75 cm. for 3–20 minutes every few days. Exposure of infants to direct sunlight for a period of three to four weeks results in calcification of the epiphyses and general improvement of condition. Controls were made with unexposed infants receiving the same diet. The seasonal variation of rickets may be due to the variations in the amount of sunlight. C. G. L. W.

Finks, A. J., and **Johns, C. O. Studies in nutrition. VIII. The nutritive value of the proteins of tomato-seed press-cake.** *Am. J. Physiol.*, 1921. **56**, 404.

In the manufacture of tomato catsups, soups, and pastes large quantities of tomato seeds and skins are discarded as useless by-products. It has been estimated that 1,500 tons of dried tomato seeds could be obtained annually in the United States. The seeds contain 22 per cent. of an oil suitable for table use, the remaining press-cake contains 37 per cent. of protein. The proteins of this press-cake are efficient for the normal growth of rats, and as a protein concentrate the press-cake is as valuable as the press-cakes from pea-nut, soy-bean or coco-nut. The tomato-seed press-cake also contains the water-soluble vitamin B, and probably also the fat-soluble vitamin A. W. C.

Ruotsalainew, A. Zur Kenntnis des Eiweissansatzes beim Kinde. [**On the retention of protein in the child.**] *Skandin. Arch. f. Physiol.*, 1921, **41**, 33.

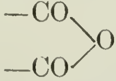
Metabolism experiments were carried out on two boys aged 9 and 10 years respectively. The experiments were so arranged that to a constant basal mixed ration of protein, carbohydrate, and fat was added either protein or fat or carbohydrate in isodynamic proportion, so that the caloric value remained constant. The object was to determine how the N-retention of the growing child was affected by altering the relative proportions of proteins, carbohydrates, and fats while keeping the total caloric value at a constant figure. Earlier investigators had concluded that the N-retention was favoured by the addition of carbohydrate, but was not affected by the further addition of protein. The present experiments show, on the contrary, that the N-retention is greatest after the further addition of protein, so that the absolute amount of protein in the diet is of great importance in determining the protein retention in the growing child. There are also observations on the Ca, Mg, and P_2O_5 metabolism.

In these experiments the vitamin factor, which is known to have a profound effect on the protein retention by the growing organism, is completely neglected. Following the usual routine of such experiments, the foodstuffs were selected in such a way as to give a constant composition of the food in order to reduce the number of analyses to a minimum. In order to attain this object margarine was used instead of butter, condensed milk instead of milk, sugar supplied a large part of the carbohydrate, and a protein preparation a large part of the protein. The diet was apparently poor in both the fat-soluble and the water-soluble vitamin. This fault takes away from the value of these observations as a contribution to the practical problem of the nutrition of the growing child. W. C.

Edie, E. S. A note on the question of the identity of gastric rennin and pepsin. *Bio-Chem. J.*, 1921, **15**, 507.

Experiments with extracts of the gastric mucosa of new-born and adult rabbits show that no pepsin is present in the stomachs of the former and no rennin in the stomachs of the latter. C. G. L. W.

Fränkel, S., und **Feldsberg, E.** Über eine neue Funktion des tryptischen Fermentes (Anhydrase) und über die Darstellung von d-Tryptophananhydrid und d-Tyrosinanhydrid aus den tryptischen Verdauungsprodukten. [**On a new function of the tryptic ferment (anhydrase) and on the preparation of d-tyrosin-anhydride and d-tryptophane-anhydride from the tryptic digestion products.**] *Biochem. Ztschr.*, 1921, **120**, 218.

When tryptic digests of casein are left for some time in the preparation of tryptophane, the bromine reaction for tryptophane is found to disappear. This has been hitherto unexplained. The disappearance of tryptophane is shown in this paper to be due to a synthesis of an anhydride in which two molecules of tryptophane become linked together with the elimination of water, as follows  $\left.\begin{array}{l}-\mathrm{CO}\\-\mathrm{CO}\end{array}\right\rangle\mathrm{O}$. A similar body is formed by prolonged tryptic digestion from tyrosine. It therefore appears that a synthetic function has been discovered for trypsin, which, if proven to occur also *in* *vivo*, should be of some importance. It is interesting that dextro-rotatory tyrosin and tryptophane anhydrides are formed from the laevo-rotatory acids. R. A. P.

Edie, E. S. Further observations on the digestion of fibrin and caseinogen by trypsin. *Bio-Chem. J.*, 1921, **15**, 498.

Comparative experiments with the same ferment solution show that caseinogen and fibrin behave differently. The amount of acid which will inhibit digestion in one will be insufficient in the other. The experiments point to there being a number of enzymes in a solution of 'trypsin', or that, if only one enzyme is present, different parts of the molecule exercise specific functions. C. G. L. W.

Ivy, A. C., and Oyama, Y. Studies on the secretion of the pars pylorica gastri. *Am. J. Physiol*, 1921, **57**, 51.

An operation was devised by which in dogs the pyloric portion of the stomach was isolated as a pouch with or without nerve-supply intact. A study of the secretion of the pyloric portion of the stomach obtained under these conditions has given the following results, which differ in many important respects from the usually accepted statements.

The secretion is mucoid, viscous, transparent, and slightly salty in taste. It is slightly alkaline (P_H 7·00 to 7·50). The rate of formation varies from 1·0 to 5·0 c.cm. per hour and is not increased by meals, water-drinking, or secretagogues. Acids and irritants, when applied to the mucous membrane, excite the secretion.

The secretion contains neither enzymes nor an antipepsin nor a secretagogue for gastric secretion. In fact the secretion of the pyloric gland is simply mucus, a conclusion identical with that arrived at by Bensley from a histological study. It contains no substance that is of specific digestive importance. W. C.

Heinberg, M. E. The gastric juice in pancreatic diabetes. *Am. J. Physiol.*, 1921, **56**, 371.

In four dogs with Pavlow stomach pouches the secretion of the gastric juice was studied before and after total pancreatectomy. In the first two hours the secretion of the gastric juice is less in the pancreatectomized animal; later on the quantity secreted is increased and the active secretion period is prolonged. The pepsin concentration of the gastric juice is greatly increased and so is the total quantity of gastric juice secreted. The acidity in pancreatic diabetes does not differ from the normal.

In all dogs a typical severe gastritis developed after total pancreatectomy. W. C.

Wiggers, C. J. Studies on the consecutive phases of the cardiac cycle. I. The durations of the consecutive phases of the cardiac cycle and the criteria for their precise determination. *Am. J. Physiol.*, 1921, **56**, 415.

The consecutive phases of the cardiac cycle were studied by means of optical manometers inserted into the cardiac chambers and the central arteries. The movements of the mirrors on the manometer were recorded photographically by beams of light reflected on moving bromide paper. An analysis of real optical pressure-curves from a total of over 200 dogs led to the following interpretations of the consecutive phases of the ventricular cycle, which are given in the author's own words:

1. At the beginning of ventricular systole, the a.-v. valves have been partly floated into apposition, probably in consequence of the sudden cessation of a jet when the peak of the intra-auricular pressure-curve is reached about the middle of the auricular systole. The first elevation of intraventricular pressure firmly closes these valves and the ventricle then contracts absolutely isometrically. *This first phase of ventricular systole extending from the beginning of the pressure rise until the opening of the semilunar valves is preferably considered as the isometric contraction phase.* The predominant durations of this phase range from 0·048 to 0·05 second when the chest is intact, and from 0·045 to 0·05 second when the heart is exposed.

2. As soon as intraventricular exceeds intra-aortic pressure, the semilunar valves open and a comparatively large volume of blood is ejected. As long as the volume ejected remains greater than the outflow from the peripheral arterioles, the aortic pressure continues to rise. This marks a *second phase of maximum ejection.* As soon, however, as the systolic ejection decreases enough so that it no longer equals the peripheral outflow, then the aortic pressure begins to decline. This *third phase* when present may be designated as the phase of *reduced ejection.* This terminates the period of systole. The absolute and relative durations of these phases vary considerably, the greatest variations in closed chest experiments being 0·05 to 0·11 second for the maximum ejection phase and 0·063 to 0·144 second for the reduced ejection phases.

3. When ventricular relaxation begins, aorta and ventricles are still in communication. The first event, viz. the closing of the semilunar valves, is signalled by a sharp drop in aortic and intraventricular pressure, designated as the incisura. This marks the *fourth* or *proto-diastolic phase.* This phase is relatively constant, averaging 0·022 second in closed chest experiments and 0·025 second when the heart is exposed.

4. Following closure of the semilunar valves and until the a.-v. valves have opened, the ventricle relaxes without any flow of blood either from or into its cavity. This marks the *fifth phase* or that of *isometric relaxation.* The predominant duration of this phase in exposed hearts is 0·06 to 0·07 second but is predominantly shorter in animals with thorax intact, ranging from 0·048 to 0·05 second.

5. With the opening of the a.-v. valves and until either an equalization of pressure between auricle and ventricle has taken place or a subsequent systole interrupts the filling, a rapid filling of the ventricles takes place. This is the *sixth phase,* conveniently designated as the *rapid inflow phase.* This phase averages from 0·048 to 0·05 second in closed chest experiments, and from 0·06 to 0·07 second in exposed hearts.

In long cycles, and when the auricular pressure is normal, a period of reduced filling obtains which may be designated, after Henderson's suggestion, as *the phase of diastasis.* Its duration is obviously dependent on the length of total diastole.

7. Finally there may be added an *eighth phase* during which the dynamic interval of auricular systole affects the filling or pressure of the ventricles. This does not continue until the end of auricular systole, however, but a terminal phase of auricular systole in which no dynamic effect

can be exerted exists before the entire cycle is completed. The predominant durations of the *total phase of auricular systole* average 0·07 second in exposed hearts, and 0·085 second in hearts enclosed within the thorax.

W. C.

Wiggers, C. J. Studies on the consecutive phases of the cardiac cycle. II. The laws governing the relative durations of ventricular systole and diastole. *Am. J. Physiol.*, 1921, **56**, 439.

Since previous observations had indicated that the duration of systole is not determined entirely by the length of previous diastole, an investigation was undertaken to determine what other factors might be concerned. The observations were made on the intact animal. The duration of the phases of the cardiac cycle was determined by the optical method referred to in the preceding paper. The conclusions which were reached are given in the author's own words:

1. An increase in venous return above normal causes a lengthening of ventricular systole, quite independent of diastole length. This occurs as a result of the prolongation of the ejection phases, the isometric phase of contraction having a tendency to be abridged. Since the initial pressure was always elevated when this occurred, we may formulate the conception that, whether or not the mechanical energy liberated by contraction is fundamentally determined by the initial length of the ventricular fibres at the inception of contraction, the duration of systole, at constant heart rates, varies directly as the initial intraventricular pressure under such a variety of inflow conditions as it is possible to produce in the mammalian heart *in situ*.

2. An increase in arterial resistance acts to abbreviate systole, independently of changes in diastolic length. This abbreviation of systole takes place in spite of a slight tendency of the isometric phase to lengthen and is therefore due to a shortening of the ejection phase. This shortening of the contraction phase is apparently due, as in skeletal muscle, to the fact that the muscular shortening is terminated earlier by the greater load acting during the process of shortening.

3. When the increase in arterial resistance is of such grade and type that the ventricle cannot empty itself effectively, a marked retention of blood occurs, and the diastolic volume and initial tension increase, in consequence. As such an increase in initial pressure has a tendency to lengthen systole, two opposing influences come into operation in such elevation of arterial resistance, viz. (*a*) the tendency of higher arterial resistance to abbreviate; and (*b*) the tendency of increased initial tension to lengthen systole. Both factors, no doubt, operate to influence the duration of systole whenever the arterial resistance is increased, but one factor usually predominates. When arterial resistance increases as a result of intense peripheral vasoconstriction, systolic retention is not pronounced and initial tension only slightly increased. Consequently the first factor predominates, and systole decreases. When the aorta is stenosed, the accommodative capacity of the aorta is reduced and large volumes of blood are retained within the ventricle, consequently the initial tension increases very markedly. The second factor then predominates and systole lengthens. When the elasticity of the arterial system or the calibre of the vessels is insufficient to accommodate readily the systolic volume expelled by the ventricles, an increase in peripheral resistance may also act to elevate initial tension and

lengthen systole. This explains the lengthening of systole consistently found by Patterson, Piper, and Starling in the heart-lung preparation, and we may expect to find such lengthening also in arteriosclerosis involving the larger vessels.

4. The duration of systole is determined solely by changes in the length of previous diastole only when the initial intraventricular pressures and the aortic pressure at the beginning of diastole remain nearly constant. Thus we find that, during vagal slowing and during the acceleration subsequent to such stimulation, the duration of systole is predominantly determined by changes in initial pressure, rather than the length of preceding diastole. Again, when slowing occurs in association with an elevation of arterial resistance, as during asphyxia or epinephrin, the duration of systole may be abbreviated through the influence of such higher resistance. There is evidence also that in the case of adrenalin action or stimulation of the accelerator nerves, there is a specific effect on the ventricle which acts independently of these influences to shorten the contraction phase.

5. These observations indicate that not only under abnormal conditions of venous and arterial pressures, but also under such conditions as may be considered quite normal, the systolic portion of the ventricular volume curves cannot be regarded as superimposable at different rates of beat.

6. Since the phases of diastole alter so little in duration, however, during the most diverse conditions of the circulation, it is not possible from these observations to draw the same deductions in regard to the superimposability of diastolic portions of the volume curves. W. C.

Haggard, H. W. Studies in carbon monoxide asphyxia. I. The behaviour of the heart. *Am. J. Physiol.*, 1921, **56**, 390.

Death under carbon monoxide asphyxia is due to failure of respiration, and is in the nature of a fatal apnoea vera. The anoxaemia resulting from the formation of CO haemoglobin induces excessive breathing and respiratory failure follows the excessive loss of CO_2.

The impairment of auriculo-ventricular conduction which leads to heart-block is not due to a direct toxic action of the carbon monoxide on the cardiac conducting system. Nor is it due to the oxygen deficiency caused by the combination of haemoglobin with carbon monoxide. It only develops after the great oxygen deprivation caused by failure of respiration.

Inhalation of 8 to 10 per cent. CO_2 in oxygen after complete respiratory failure with heart-block had developed, given at first by artificial respiration and then under spontaneous respiration stimulated by the CO_2, has led to complete restoration of cardiac conduction in two out of three animals. Illuminating gas (coal gas plus fattened water gas) results in an earlier development of respiratory failure than pure carbon monoxide in corresponding concentration. W. C.

Greene, C. W., and Gilbert, N. C. Studies on the responses of the circulation to low oxygen tension. V. Stages in the loss of function of the rhythm-producing and the conducting in the human heart during anoxaemia. *Am. J. Physiol.*, 1921, **56**, 475.

Observations on a normal man who was subjected to an extreme oxygen deficiency in a rebreathing test. The final oxygen was 7·1 per cent. when the subject became unconscious. Electrocardiograms were taken during the experiment, at first at intervals and continuously during the last stage of the test.

The records show that in man lack of oxygen induces a series of changes in cardiac rhythm, in conduction and in suppression of auricular contractions parallel to similar phenomena established in experimental animals under general asphyxiation. These changes are discussed in detail. W. C.

Warburg, O. Physikalische Chemie der Zellatmung. [**Physical chemistry of cell respiration.**] *Biochem. Ztschr.*, 1921, **119**, 134.

This paper attempts to relate the respiration of the cell to known physical and chemical facts. By freezing blood-cells and so separating their constituents, it is shown that the part of the cell which respires is the solid part. Various substances of a narcotic character inhibit the respiration of the cell. This is apparently a question of their being adsorbed upon the surface of some of the solid parts of the cell. It is also found that the more readily the body is taken up from an aqueous solution by the cell constituents, the lower is the concentration required to inhibit respiration. As regards Traube's view, it is shown that only where a series of similarly constituted bodies are taken is it fair to say that solutions of the same surface tension have the same narcotic power upon the cell. For bodies where there is divergence of chemical type, such as the case of thymol and urethanes, it does not hold at all.

Warburg holds that the catalyst for oxidation in the cell is iron. HCN inhibits respiration when it is in a concentration sufficient to combine with the iron of the cell. Upon this view the narcotics which interfere with cell respiration act by occupying the catalytic surface. He has been able to demonstrate this type of effect with blood charcoal. Narcotics will inhibit the oxidation of oxalic acid, for instance, by blood charcoal. This is held to be a question of the adsorption of the narcotic by the charcoal surface and the consequent displacement of oxalic acid.

It is difficult to believe that the cell oxidations are really quite as simple as this view would force us to hold, but it is interesting to find an attempt of this kind to link up the modern ideas of surface action, with respiration. R. A. P.

Creveld, S. Van, und **Brinkman, R.** Ein direkter Beweis für die Impermeabilität der Blutkörperchen des Menschen und des Kaninchens für Glucose. [**A direct proof of the impermeability of the human and rabbits' red blood-corpuscles for glucose.**] *Biochem. Ztschr.*, 1921, **119**, 65.

This is a further proof of the work published by Brinkman and Dam, and also of Falta and Richter-Quittner in 1919. If care is taken to prevent the initiation of clotting in the blood, both human and rabbits' red blood corpuscles will be found to be free from glucose. The rabbit's blood was taken from the jugular vein, and the human blood collected in a paraffined tube. This removes any possible objection from the use of hirudin.

Though there will be found abstracts in this journal of papers in which authors have drawn the opposite conclusions, it seems hard to escape from the experimental evidence upon which the above work is based.

R. A. P.

Hattori, K. Kolloidstudien über den Bau der roten Blutkörperchen und über Hämolyse. III. Ultramikroskopische Untersuchungen an Lipoiden. **[Colloid studies upon the structure of red blood corpuscles and upon haemolysis. III. Ultramicroscopic experiments upon lipoids.]** *Biochem. Ztschr.*, 1921, **119**, 45.

The behaviour of lecithin and cholesterin, both singly and as mixtures, has been studied under the ultramicroscope under various conditions. Lecithin will swell in water, cholesterin will not. The two substances will form an optically homogeneous mixture, which swells in a salt solution in a greater or less degree according as it contains a preponderating amount of lecithin. Cholesterin acts as a preventive of swelling. Such optically homogeneous mixtures can be disintegrated with various reagents, but the disintegration takes place in various ways. For instance, water swells the lecithin so much that it is no longer able to hold the disperse cholesterin phase in solution. Agents which disintegrate the lecithin-cholesterin mixture also are haemolytic, though the reverse does not hold. The effect of salts is a question of their specific nature as well as their osmotic concentration. It is interesting that there should be such close correspondence between certain phases of cell behaviour and the simple lipoid mixture. R. A. P.

Dudley, H. W., and **Evans, C. L. A method for the preparation and recrystallization of oxyhaemoglobin.** *Bio-Chem. J.*, 1921, **15**, 487.

Defibrinated horse-blood is centrifuged and the corpuscle paste washed with isotonic saline. The paste is then dialysed in collodion sacs and the contents poured off from any sediment. The mixture is converted into oxyhaemoglobin by passing in oxygen, and crystallization takes place. By converting into reduced haemoglobin and precipitating with oxygen, purification can be further made. This method avoids any contact of the protein with alcohol. C. G. L. W.

Evans, C. L. The regulation of the reaction of the blood. *J. Physiol.*, 1921, **55**, 159.

An elaborate piece of work on the subject, not suitable for abstraction. O. L. V. de W.

Haldane, J. B. S. Experiments on the regulation of the blood's alkalinity. *J. Physiol.*, 1921, **55**, 265.

The author has produced marked and prolonged acidosis in man by feeding large quantities of NH_4Cl. The usual chemical phenomena in expired air, blood, and urine followed—diminished alveolar CO_2, fall in CO_2 capacity of the blood, and increased excretion of NH_3, acid, and phosphates. Attempts to produce an acidosis by administering large quantities of dilute HCl, and of NaH_2PO_4, were unsuccessful. The author believes that part of the NH_3 is converted in the liver to urea, and the acid liberated. A fall of alveolar CO_2 was noted within 20 minutes of the administration of the salt. The rise in the urinary ammonia was considerable, but it was not all excreted as a chloride, less Cl being present in the urine than was required to satisfy the ammonia present. Phosphate excretion at first rose and then fell, suggesting that a shortage of phosphates had been produced in the body.

The depression of alveolar CO_2 was accompanied by marked air hunger, and, below a certain value, is roughly proportional to the rate of excretion of acid and ammonia. O. L. V. de W.

Meissner, R. Zur Beschleunigung der Blutgerinnung durch Euphyllin. [**On the quickening of the blood-coagulation by euphyllin.**] *Biochem. Ztschr.*, 1921, **120**, 197.

Nonnenbruch showed that an injection of euphylline (theophylline-ethylene-diamine) into the blood was followed by a quickening of the coagulation time. Meissner has experimented upon rabbits to find out whether the effect is due to the purine or diamine component. He finds that both groupings have the effect, but that the compound has a greater one. It is apparently not a question of alkalinity. R. A. P.

Henriques, V., und **Ege, R.** Vergleichende Untersuchungen über die Glucosekonzentration in dem arteriellen Blut und in dem venösen Blut aus den Muskeln. [**Comparative experiments upon the concentration of glucose in the arterial and venous blood from the muscles.**] *Biochem. Ztschr.*, 1921, **119**, 121.

The difference in the concentration of glucose in arterial and venous blood, though small, is detectable. In the case of animals which had been starved for a day it was found to be of the order of 0·004 per cent. lower for the venous blood. Upon theoretical grounds it is to be expected that the difference in the amount of sugar found respectively in the arterial and venous bloods would vary not only with rest and activity, but also with the condition of the animal. Under some conditions sugar will be carried by the arteries for storage in the muscles. Under others, sugar will be transported from the glycogen stores in the muscles for use in other parts of the body. This would lead under some circumstances to the presence of more glucose in the venous than in the arterial blood. It is gratifying to find that the authors have been able to realize experimentally the theoretical conditions.
R. A. P.

Yates, A. B. **The mechanism of the recovery or maintenance of systemic blood-pressure after complete transection of the spinal cord.** *Am. J. Physiol.*, 1921, **57**, 68.

In cats in which a complete transection of the spinal cord has been made recovery of the blood-pressure occurs, if the level of transection does not lie above the level of outflow of the thoracic sympathetic chain. The mechanism through which recovery is brought about includes the cardio-vascular mechanism in the medulla and the outflow from the centre which includes the extrinsic cardiac nerves and the vasomotor nerves. The vasomotor outflow is of greater importance. The experiments do not support the view that there are special vasomotor centres functionally active and co-ordinate in rank with the mechanism in the medulla oblongata. The bulbar vasomotor mechanism is the chief mechanism upon which the functional activity of all other parts of the vasomotor system depends.
W. C.

MUKAI, G. A method of protein removal from body fluids for the purpose of simultaneous determination of many constituents. *Bio-Chem. J.*, 1921, **15**, 516.

Treatment of the serum with a feebly acid solution of sodium acetate, followed by shaking with talcum, completely removes all proteins.

The filtrate may be used for the determination of non-protein nitrogen, glucose, or chlorides. C. G. L. W.

KENNAWAY, E. L. The estimation of non-protein nitrogen in blood by micro-Kjeldahl method. *Bio-Chem. J.*, 1921, **15**, 510.

Blood serum is de-proteinized with methylated spirit, and the filtrate oxidized with a special mixture of sulphuric acid and potassium and copper sulphates. The ammonia is removed by a current of air. Attention is directed to (1) the use of a metal bath in combustion; (2) the method of making the fluid alkaline after combustion. C. G. L. W.

MEIER, K., und **KRÖNIG, W.** Blutgasanalysen. Narkose und Kolloidal-Ladung. [**Blood-gas studies. Narkosis and colloidal charge.**] *Biochem. Ztschr.*, 1921, **119**, 1.

This is a case of the parallelism between the effect of narcotics and of certain salts upon the permeability of the blood-cell. The reaction used in the experiments is one described by Straub and Meier. Red blood corpuscles are suspended in isotonic saline, and exposed to increasing pressures of CO_2. If the curve is plotted which relates increasing pressure of CO_2 to the amount of CO_2 taken up, it is found that there is at first a gradual increase in the amount taken up with increasing pressure. There is then a plateau reached, after which practically no change takes place until a definite P_H is reached. At P_H 6·67 there is a sudden bend in the curve indicating the taking up of CO_2 by the cell. The point at which this bend (Knick) occurs can be altered by placing the cells in other solutions than sodium chloride. The experiment is interpreted to mean that there is first a gradual action upon the surface colloids until an iso-electric point is reached, when the cell becomes suddenly permeable. The paper here shows that methyl urethane, ethyl urethane, and ethyl alcohol change the 'Knick' point to the alkaline side (P_H 6·8–6·9) when used in narcotic concentrations in the saline solution. In weaker or stronger amounts the effect is not obtained. It seems, then, that there is some special effect of the narcotic upon the permeability of the surface, though the mechanism of the effect is left quite unexplained.

R. A. P.

GULLICHSEN, R., und **SOISALON-SOININEN, J. L.** Über die Kohlenstoffabgabe des Menschen beim Fechten und Ringen. [**On the carbon excretion of man in wrestling and in fencing.**] *Skandin. Arch. f. Physiol.*, 1921, **41**, 188.

Observations on six persons in the respiration chamber on the energy liberated in fencing and in wrestling as measured by the CO_2 excretion. The results show that the muscular work involved in these exercises is of a very high order of magnitude when compared with other occupations involving heavy work. W. C.

Burge, W. E., and **Leichscuring, J. M.** **The mode of action of low temperatures and of cold baths in increasing the oxidative processes.** *Am. J. Physiol.*, 1921, **56**, 408.

Morgulis, S. **Is catalase a measure of metabolic activity?** *Am. J. Physiol.*, 1921, **57**, 125.

Burge has put forward the suggestion that there is a direct relationship between the amount of the ferment catalase, which has the property of liberating oxygen from hydrogen peroxide, and the metabolic activity of living tissues. He has tried to support this view by a number of experimental observations which show, as he claims, that whatever increases oxidation increases the output of this enzyme from the tissues, particularly the liver, and whatever decreases oxidation, narcotics, for instance, produces a decrease in catalase by decreasing its output from the liver and by direct destruction.

In the present paper he concludes that low temperatures and cold baths produce an increase in the blood catalase of warm-blooded animals, and a decrease in cold-blooded animals. The increase in oxidation in warm-blooded animals on exposure to cold is attributed to an increase in catalase, the decrease in oxidation in cold-blooded animals to a decrease in catalase.

The views and experimental technique of Burge are subjected to a severe criticism in the paper by Morgulis. He points out that several authors failed to confirm Burge's results on repeating his experiments. Further, the blood catalase is, even in normal animals, subject to enormous variations (about 1,000 per cent.). Morgulis has carried out observations on the catalase content of frogs kept at widely varying temperatures. This, although it changes the metabolic rate from 300 to 400 per cent., had no influence on the catalase content of the frogs. It follows, therefore, that whatever the function of catalase in the organism may be, it is certain that it is not a measure of metabolic activity. W. C.

Wallrich, L. A., and **Dawson, P. M.** **The effect of short spells of rest on physical efficiency as measured by a bicycle ergometer.** *Am. J. Physiol.*, 1921, **56**, 460.

When exercise is heavy efficiency is increased by spells of rest. When exercise is light efficiency is decreased by spells of rest. W. C.

Embden, G., **Grafe, E.**, und **Schmitz, E.** Über Steigerung der Leistungsfähigkeit durch Phosphatzufuhr. [**Increase in capacity for work due to administration of phosphate.**] *Ztschr. f. physiol. Chem.*, 1921, **113**, 67.

Experiments on soldiers and miners showed that the administration of 7·5 gm. of sodium dihydrogen phosphate per day resulted in an increased capacity for muscular work, presumably by facilitating the resynthesis of 'lactacidogen'. A favourable effect on the nervous system is also claimed.
H. W. D.

RADIOLOGY

Radiodiagnosis

Zumpe, R. Die Veränderung des Blutbildes und ihre prognostische Bewertung in der Strahlentherapie des Karzinoms. [B.] [**Variations of the blood-picture and their prognostic value in the treatment of carcinoma by rays.**] *Strahlentherapie*, 1921, **12**, 696.

The author points out that the statement is often made in recent literature that changes in the blood-picture (particularly lymphopenia or lymphocytosis) are to be regarded as of prognostic value in the radiation treatment of carcinoma. He proceeded to examine the question by means of blood examinations on carcinomatous cases in the University clinic for diseases of women and the Institute for cancer research at Berlin. His controls were irradiated normal persons and patients with myomata. After an historical survey and a description of the methods he employed, including Schilling's modification of Arneth's method which attributes a special diagnostic and prognostic value to nuclear position in the neutrophils, he refers to the haemal modifications to which most attention was paid. These, and other indications show that the work has been carried out with considerable regard to the many factors concerned in blood-work of this description. Thus he finds variations in the blood-picture according to the region of the body irradiated (pelvis, head and neck, thorax). The findings in numerous cases under different conditions are detailed and the conclusions are drawn: (1) that blood changes under irradiation generally aid diagnosis provided attention be paid to the influence of constitutional anomalies of accompanying diseases such as tuberculosis, of the disease itself, and of the kind and situation of the irradiation. He thinks that Schilling's 'thrust of the neutrophil nucleus to the left' is not a specific sign of carcinomatosis, but in advanced cases under certain circumstances is very common; (2) that the action of therapeutic irradiation doses upon the blood and haemopoietic organs may be direct or indirect; (3) that a lymphocytosis supervening upon an initial lymphopenia is not invariably favourable, and (4) that the degree of leucopenia after irradiation is dependent upon the vascularity of the irradiated region, the richness of the irradiated area in young blood cells, i.e. haemopoietic organs, and the dose of irradiation. The work appears to have been carried out with care, but the factors concerned are so numerous that general and limited conclusions alone can be made. It is doubtful, if we may judge from the numerous publications that have appeared on the subject, whether any material advance will be made in the applicability of blood examinations to the clinical picture of cancer—whether under irradiation treatment or not—until some new method has been devised for attacking the problem. W. S. L.-B.

Warnekros, K. Schwangerschaft und Geburt im Röntgenbilde. [**Radiography of pregnancy and labour.**] *Ztschr. f. Geburtsh. u. Gynäk.*, 1918, **80**, 719. (*J. de radiol. et d'électrol.*, 1921, **5**, 232.)

In the absence of mechanical disproportions between the foetus and the uterus and of foetal or maternal anomalies, the head remains in a position of semi-flexion without any strain, the vertebral column moulds its curvature to the ellipsoid of the uterus; the limbs are in neither a strained nor typical position, their position solely depending on the free space available. Every deviation from this normal position should make one think of an anomaly. Even during labour the presentation may alter. During expulsion, under these normal conditions, the head passes into the pelvic canal without increased flexion. Extreme flexion is produced when internal rotation begins; the increased flexion is clearly due to the pressure coming from the fundus of the uterus and transmitted by the vertebral column which pushes on the occiput. Internal rotation is brought about by the muscles of the pelvic floor. When the head has been born, contrary to the general opinion, the shoulders are always transverse in their normal position with reference to the head: there is no twisting. The thorax is compressed in a circular manner and probably the first inspiration is brought about by the spontaneous expansion of the thorax after escaping from this pressure.

P. L.-B.

Haret et **Grunkraut**. De la pelvimétrie par la radioscopie. [**Pelvimetry by radioscopy.**] *Presse méd.*, 1920, Oct., 756. (*J. de radiol. et d'électrol.*, 1921, **5**, 185.)

By a simple radioscopic process, without special apparatus, without correcting the pelvimetric image, and without calculations, this method enables one to measure the different diameters of the pelvis. It consists of measuring on the screen the lengths of these diameters whose extremities have been determined by orthodiagraphy. Certain osseous points are sufficiently visible on the screen, and others are determined by placing metallic disks on the skin. The difficulty of the method consists in appreciation of the parallelism between the plane of the screen and the plane containing the diameter examined. The authors have rendered this control easy and exact by using Strohl's method of localization; this method enables one to recognize quickly and very exactly, whether the different points picked out are at equal distances from the screen, i. e. in a plane parallel to it. The operation is done in two parts, the different diameters of the pelvis being contained in two different planes.

S. U. L.-B.

Weibel, W. Studien über die Nachgeburtsperiode auf Grund röntgenographischer Darstellung. [**Study of the third stage of labour by radiography.**] *Arch. f. Gynäk.*, 1919, 413. (*J. de radiol. et d'électrol.*, 1921, **5**, 232.)

Out of 41 attempts to radiograph the placenta, 28 were successful. The author, moreover, claims priority over Warnekros. The opinion that separation of the placenta begins during the expulsion of the child is untenable. In a normal labour, as soon as the child has been expelled, the placenta is found to be still completely attached; separation begins at once either from the edge or from the centre, or perhaps in certain cases from the whole surface. On passing down it reaches the neck of the uterus with the edge in front: the manner in which it appears at the vulva does not depend on the manner in which it separated, but on the way it passes down the vagina.

P. L.-B.

Radiotechnique

Hirsch, I. S. The heart in relation to habitus and a new method of estimating morphological changes. *Arch. Radiol. & Electroth.*, 1921, **26**, 10.

The author begins by saying that experience has shown that there is no absolute 'normal' standard for the organs of the body. He describes in detail the classification of Mills of the four major types of general physique, the hypersthenic, the sthenic, the hyposthenic, and the asthenic. He describes how the morphology and size of the heart depend on habitus, and as regards the latter point brings forward figures to show that previous standards are of little value, but that when considered in conjunction with the habitus valuable clinical information may be obtained. He points out that a thickening of the heart wall may occur without any change in the numerical diameters of the heart, but that if the curves of the chambers of the heart be measured a change can easily be seen, and that the values of the curves of the heart vary with the habitus, and that for each habitus there is a definite radius. The author comes to the following conclusions:

(1) The position and shape of the heart varies with the habitus.

(2) That habitus must be considered in estimating cardiac size.

(3) That cardiac function, especially as regards tonus, may perhaps vary with the habitus.

(4) That only by actual measurements of the curves of the heart can changes be made out in early cases, and that these vary with the habitus.

(5) That the radial measurements are a more accurate and valuable expression of change in the heart chambers than the so-called standard measurements.

P. L.-B.

Félix, A. Dispositifs de protection contre les rayons du radium à l'usage des radium-manipulateurs. [**The protection of radium manipulators against the rays of radium.**] *J. de radiol. et d'électrol.*, 1921, **5**, 61.

The protective measures dealt with group themselves under two headings, first the systematic keeping of the active substance as far away from the skin and body as possible, and secondly the use of metallic screens to absorb as much as possible of the radiation. The efficiency of the latter methods depends on the fact that it is the soft and most easily absorbed rays which are responsible for the greatest damage.

M. Felix describes a series of surgical forceps adapted for the handling of tubes of radium and radium emanation, a simple and easily made carrying and storage tube lined with lead, and a type of working table built with two thick sheets of lead between oak boards, and having a vertical shield at one side similarly protected. The operator works with his arms round the side of the shield, his body being well protected.

B. D. W.

Russ, S., and **Clark, L. H. Some physical considerations in radiotherapy.** *Proc. Roy. Soc. Med.*, 1921, **14** (Sect. Electrotherap.), 1.

The authors approach the problem of deep therapy with the postulate that the desideratum in the irradiation of a tumour is that all parts of the tumour receive, as nearly as possible, the same amount of radiation and, if possible, the lethal dose for the tumour in question.

Two methods of irradiation of a tumour, situated 1 cm. below the surface and of thickness 8 cm., are considered. The intensity of X-rays (I_d) at a layer of tissue below the surface a distance (d) is related to that at the surface layer by the expression $I_d = I_o \epsilon^{-\lambda d} \left(\frac{x}{x+d}\right)^2$ where (x) is the distance from the anode to the surface and λ is the absorption coefficient of the X-rays in the tissue.

In the first method of irradiation use was made of the radiation from a bulb run at an alternative spark-gap of 15 cm. (100,000 volts), lightly screened by 1 mm. of aluminium, the focus-skin distance being 15 cm. The value of λ varied from 0·138 to 0·092 cm^{-1}. In this case it was found that the intensity 10 cm. below the surface was only 7 per cent. of that at the surface.

For the second case a very hard bulb was used, 32 cm. alternative spark-gap (180,000 volts), the radiation being screened by 10 mm. of aluminium. The focus-skin distance was 30 cm. and $\lambda = 0{\cdot}085\ \text{cm}^{-1}$. At 10 cm. below the surface the radiation had fallen to 24 per cent. of the surface value.

Both methods show that the approach to uniformity still leaves much to be desired, although the technical conditions, apart from an increase in the focus-skin distance, are about the limit of what is realizable at the present day.

Greater uniformity is obtained by the choice of various ports of entry through the skin, but there are reasons for restricting the irradiation of large areas of normal tissues. Consideration of the above algebraical expression shows, however, that the more penetrating the radiation used, the less does (I_d) vary from I_o. Further, for uniformity, x should be very much larger than d. As the factor $(x/x+d)^2$ is only true if the anode approximates to a point source of radiation, experiments were made to determine the fall of intensity with distance from radio-active, disk sources of 2, 4·4, and 11·5 cm. diameter.

The sources of radiation were placed in turn at distances ranging from 15 to 35 cm. from an electroscope possessing a shallow cylindrical ionization vessel, the depth and diameter of which could be varied. The curves obtained with the above sources showed that, as the size of the source increased, the fall of intensity with increase in distance from the ionization chamber becomes less rapid. Walsh had obtained a similar result from theory. Assuming that a disk of radius (R) radiated according to the Cosine Law, he found that the fraction of the whole downward radiation from it, which was received by a parallel coaxial disk of radius (r) at a distance (a), was given by the expression

$$\left[(R^2+r^2+a^2) - \sqrt{(R^2+r^2+a^2)^2 - 4r^2R^2}\right] / 2\,R^2.$$

Assuming that the same law of radiation held for radio-active sources, it was shown that: (1) it is necessary to use a radiating source of the same area in juxtaposition in order to produce the maximum intensity at a given region; (2) for a given distance apart the greater the diameter of the radiating disk, the less is the fraction of its total radiation incident on the receiving disk; (3) the variation in the amount of radiation received with the size of the source is considerably greater when source and receiver are in proximity. For a particular distance between the source and the area to be treated the maximum intensity is obtained by using as small a source as possible. However, the fall of the percentage radiation received, with increase in distance, is most rapid for a small source. The inference was that if uniform irradiation is desirable the small or point source is the worst to use.

Theory and experiment suggested that an X-ray tube having a large anode would be preferable to the focus tube, as it would give considerably more uniform irradiation through a given thickness of tissue.

With the aid of the foregoing data two methods of radium treatment of a localized and nearly superficial tumour were considered. It was desired to administer a lethal dose at depth of 1 cm. and over a circular area, 4 cm. diameter. The diameter of the radium source remained to be determined, a limited quantity of radium being available. In the first case, if a capsule of 1 cm. diameter was used, 74 per cent. of its total downward radiation would be received by the layer of tissue at 1 cm. depth. In the second case, if a capsule of 4 cm. diameter was used, 56 per cent. would be received by the same layer. Probably the clinician would choose the latter method, increasing his time of exposure to compensate for the reduced intensity, and thus ensure more uniform irradiation of the tissue under treatment. L. H. C.

Radiotherapy

Béclère, A. La stérilisation ovarienne en une seule séance à l'aide des rayons de Röntgen. [B.] [**Ovarian sterilization at one exposure by the help of the X-rays.**] *J. de radiol. et d'électrol.*, 1921, **5**, 67.

The critical review of Béclère traces the development of the X-ray treatment of fibromyomata from its inception by Foveau de Courmelles in 1904 to the present-day methods advocated by the late Professor Krönig and continued by Seitz and Wintz.

The chief part of the review is devoted to a critical examination of the efficacy and desirability of the German method, which consists in giving at one séance a dose of radiation which is calculated to give the desired results. From a careful examination of the publications which have issued from the Fribourg and Erlangen clinics, Béclère finds a not unimportant difference in the dose which is administered at the two institutions, for what must be considered the same object. Krönig and Friedrich estimate what they call the ovarialdosis to be 20 per cent. of the èrythemdosis, whereas the Kastrationdosis of Seitz and Wintz is 34 per cent. of this same quantity. This difference may possibly be referable to an inequality of the standard employed at the two centres, namely, the erythema dose.

The main questions raised by Béclère are two. First, can the changes in the ovary be brought about by a single application of X-rays with certainty. From an examination of published results he states that this cannot be done, and that it may therefore be necessary to repeat the exposure. The second question centres round the desirability of such single exposure methods. The economical advantage is, in his opinion, counterbalanced by the ill effects upon the patients which frequently supervene upon these prolonged exposures to X-rays, and which are not often met in the conservative method of spacing the irradiations over a considerable length of time. Béclère also discusses in some detail the arguments which have centred round the question as to whether the diminution in size of a fibroma is a sequel to the changes initiated in the ovary or whether it is due to a direct action of the rays upon the growth.

The argument is well considered and the paper is a valuable one. It contains a useful bibliography, in which we fail to find the name of a single British author. S. R.

Fuchs, H. Die ausfallserscheinungen nach der Röntgenmenopause. [**The terminal phenomena after menopause induced by X-rays.**] *Strahlentherapie*, 1921, **12**, 742.

On the basis of 69 cases the author compares the terminal condition of women in whom an artificial menopause has been produced according as that condition has followed on X-radiation, ovariectomy, or hysterectomy. The paper is entirely clinical and goes into some detail. He claims that under X-rays psychical equilibrium is better preserved, vasomotor changes are fewer, and there is less disturbance of the entire generative system.

W. S. L.-B.

Calvé, J. Traitement de l'adénite cervicale tuberculeuse. [**Treatment of tuberculous cervical adenitis.**] *L'Hôpital*, 1921, Jan., 710. (*J. de radiol. et d'électrol.*, 1921, **5**, 188.)

After insisting on the importance of general treatment, the author turns his attention to local treatment of these lesions. For this purpose he divides them as follows: micropolyadenopathy, hard monoadenitis, soft monoadenitis, fistulous adenitis, multi-ganglionar, uni- or bi-lateral adenitis. He indicates the favourite injections and passes on to the part played by radiotherapy and heliotherapy.

He finds the action 'considerable' (1) on forms called tuberculous lymphomata, single or groups of few glands without tendency to suppuration; (2) on the common bacillary gland enclosed in a sheath of periadenitis; this disappears, but the gland persists, often diminished in size; (3) action will be nil on fistulous adenitis and on small polyadenitis.

Of all the forms micro-adenitis is the least influenced, but radiotherapy gives remarkable results on open and fistulous adenitis by drying up suppuration and by producing rapid and satisfactory repair of the ulcerations. The author insists on the value of heliotherapy and clearly indicates that it is one of the chief factors in general treatment. S. U. L.-B.

Radiobiology

Cluget, Rochain, et Kofmann. Action bactéricide du radium sur le B. pyocyanique. [**The bactericidal action of radium on *B. pyocyaneus*.**] *Réunion biologique de Lyon*, 1920, Nov. 15. (*J. de radiol. et d'électrol.*, 1921, **5**, 285.)

The authors, following up their previous work enter on the crux of the question and state the two fundamental problems which dominate the whole study of the biological action of radium on a living cell. (1) What is the dose of radiation, measured by ordinary units, which comes from the tube of radium? They find that for cultures in a state of attenuation the dose at which a harmful action commences is 8,400 mgm.-hours with a platinum tube of 50 mgm. of $Ra\ Br_2\ 2H_2O$ placed in the culture. (2) What is the real value of the incident irradiation striking the culture? What is its quality or its nature? It is this knowledge alone which enables one to arrive at a fixed dose of radiant energy. Here the authors come to the conclusion that if the β-rays, produced secondarily by the walls of the tube, are eliminated harm no longer occurs. The γ-rays alone which escape from the tube, a dose of about 95 per cent. of the total radiation, are harmless. It is the absorption of the secondary β-rays which these γ-rays induce that produces the harmful action. Neither X-rays nor γ-rays have yet been used in large enough doses to arrest the growth of *B. pyocyaneus.*

P. L.-B.

Nürnberger. Über das Verhalten des Blutzuckers nach Röntgenbestrahlungen. [B.] [**On the behaviour of the blood-sugar after X-radiation.**] *Strahlentherapie*, 1921, **12**, 732.

Previous investigations upon the action of X-rays on carbohydrate metabolism have been concerned almost entirely with the excretion of sugar in diabetes mellitus. It was found that irradiation of the liver led to increased sugar excretion, irradiation of the pancreas and adrenals, to hyperglycaemia and glycosuria. On the other hand, it has been asserted that doses stimulating the pancreatic function lead to a temporary diminution in sugar output and a gradual increase of carbohydrate tolerance. The author approached the subject from purely theoretical considerations. He took it for granted that the foremost effect of X-rays is an injury to the high molecular protein of the nucleus as indicated by the recognizable histological changes, but pointed out that these also imply changes of a chemical nature. Evidence for this is given by the increased excretion of uric acid, purine bases, and phosphoric acid described by various authors. Further, Fischer has shown that the molecule of nucleinic acid contains, besides purine bases, pyrimidin derivatives and phosphoric acid, also a carbohydrate group. And since the organism has the power of removing the amine group from nitrogenous protein products (glutaminic acid, alanine) and converting them into carbohydrates, the author thought it possible that the sugar of the blood might manifest changes under the influence of X-rays. Ten cases were investigated, mainly women with haemorrhage of ovarian origin. The blood was freed from protein by the method of Rona and Michaelis, and the sugar estimations made in the clear filtrate by the Lehmann-Maquenne method. The tests were made before and for some days after irradiation, and simultaneous determination of the leucocytic count were obtained. Curves and tables of figures are given in the text. In almost all cases the amount of the blood-sugar increased to beyond the limits of the normal, and this increase coincided with a lymphopenia. It is therefore possible that the increase of sugar in the blood must be correlated with nuclear destruction, but in the absence of information as to whether the increased sugar-content of the blood is associated with increased uric acid or residual nitrogen values this conclusion, however probable, cannot be drawn with certainty.

W. S. L.-B.

Traugott, K. Ueber den Einfluss der ultravioletten Strahlen auf das Blut. [**The influence of ultra-violet rays on the blood.**] *München. med. Wchnschr.*, 1920, **67**, 344. (*J. de radiol. et d'électrol.*, 1921, **5**, 44.)

The author has studied the action of ultra-violet radiations on the numbers of the constituent cells of the blood, on their relative division, and on the coagulation time. He has tried to remove the causes of error arising from many influences capable of modifying the composition of the blood by working systematically at the same period of the day on subjects submitted to a constant diet whose temperature had been taken both before and after the exposure. Four samples of capillary blood were taken by pricking the tip of a finger, the first immediately before irradiation, the second, third, and fourth immediately after half an hour after and six hours after. Four samples of venous blood were taken from the median basilic vein at the same times.

The number of the red blood corpuscles did not appear to be altered. The same was not true of the leucocytes, the number of which generally increased after sufficiently long action of the ultra-violet rays. Among 30 cases examined after irradiation for 30 minutes an increase was clear 18 times. The 12 remaining cases were divided into 9 variations lying between the limits of possible error (variations below 7 per cent.) and 3 diminutions. The greatest increase was 61 per cent., the mean increase 33 per cent. Under these conditions there was no difference between the capillary and venous blood.

When the irradiation was of short duration, on the other hand, the capillary blood alone showed an increase in the number of the leucocytes. The venous blood was not altered in general. All the variations were the same for the different types of leucocytes. The increase was maintained and even became greater during the first half-hour, but was transient and had completely disappeared at the end of six hours. This rapid leucocytosis did not appear to be due to the mechanisms regulating the composition of the blood nor to vasomotor phenomena. It seems to be a question of a property peculiar to the nucleated cells, because of the presence of elements with high atomic weights in their constitution.

The ultra-violet rays appeared also to quicken the coagulation of the blood and to increase the number of blood platelets. In tuberculous cases they have neither an injurious nor a curative action. The stimulating properties on metabolism which are generally attributed to them are drawn from experiments *in vitro* and not from direct observations. P. L.-B.

Baumann, M. The alterations in the leucocytes after exposure to artificial sunlight of high altitudes. *Ztschr. f. exper. Path. u. Therap.*, 1920, November. (*J. de radiol. et d'électrol.*, 1921, **5**, 287.)

The researches described in this paper were carried out with the aid of a mercury vapour quartz lamp. In man an exposure for some minutes brings about an initial increase of the polynuclears with a decrease of the lymphocytes; then an increase of the lymphocytes is seen, both absolute and relative. This lymphocytosis becomes more pronounced under the influence of repeated séances at closer intervals. The eosinophils and large mononuclears also tend to increase in numbers. In the guinea-pig the modifications are more constant if care has been taken in the first place to shave the parts exposed to the rays. Thus a time action is found. After a rather long exposure (½ hour–1½ hours) the animals remain apathetic and weak for 5–6 hours: 4 out of 10 died. In all cases one can prove severe blood lesions affecting chiefly the spleen and bone marrow. The lesson to be drawn from these arguments for the practice of light-therapy is the following: care should be taken against prolonging the exposure to the rays more than a quarter of an hour, or at the most half an hour, especially if the whole body is exposed. If this rule is not adhered to, there is a risk of severe blood alterations appearing. P. L.-B.

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ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

TYPHOID AND PARATYPHOID FEVERS

Epidemiology. The ninth annual report published by the *Journal of the American Medical Association* on typhoid in the large cities in the United States shows that the disease is still decreasing at a rapid rate. Every group of cities has shared in the decline, and while the rates in the larger cities have been somewhat less than in cities with a population of less than 200,000, the difference seems to be due to geographic situation rather than to size. The view expressed in the last report (vide *Medical Science*, 1920, **3**, 199), that the drop in typhoid occurring between 1918 and 1919 was due to immunization in the army, is confirmed by additional evidence. In a number of localities it has been found that whereas before 1919 the male typhoid rate in the age-group 20–30 was somewhat higher than the female, this relation was reversed in 1919 and the female typhoid rate was much higher than the male rate for the corresponding year. The immunity conferred by inoculation persisted to a considerable degree in 1920, and as far as specific data were available showed no signs of diminution. The general typhoid death-rate seemed to corroborate this inference, since the 1920 rate fell below that of 1919 in the same ratio as that of 1918 fell below that of 1917.

The practical disappearance in France of typhoid fever in the male sex between the ages of 20 and 45 as the result of inoculation is also emphasized by leading French authorities such as Chauffard, Achard, and Sergent.

Bunn records an epidemic of 882 cases of typhoid fever occurring in the course of three months at Salem, Ohio, a city of 10,305 inhabitants, with the remarkably low mortality of 2·8 per cent. The effectiveness of antityphoid vaccination was shown by the fact that among 200 ex-service men in the town, all of whom had been vaccinated within the last three years, there were only three cases or an incidence of one in seventy, while among the entire female population between the ages of 20 and 30 the incidence was one in eight.

Wolff, who was bacteriologist to the Ninth German Army in Roumania, gives an account of an epidemic of paratyphoid which occurred among the German troops in Roumania in 1917. The epidemic started late in the summer and reached its height in October and November. The characteristic feature of the outbreak was that, though there was a simultaneous epidemic of typhoid fever, the number of paratyphoid cases greatly exceeded that of typhoid. Thus in the cases examined by Wolff there were 552 cases of paratyphoid (285 of paratyphoid B and 267 of paratyphoid A) and only 101 of typhoid. Similar observations had been made in various places on the western front. The first cases of paratyphoid B and typhoid occurred in July, and towards the end of August the first cases of paratyphoid A appeared. While the cases of typhoid and paratyphoid A kept at a low level in July, August, and September, paratyphoid B increased considerably in frequency during this period, there being 132 cases of paratyphoid B, as compared with 27 cases of typhoid and 17 of paratyphoid A during these three months. Even when allowance is made for the fact that some of the mild cases of typhoid escaped observation, there is no doubt that the number of typhoid cases was considerably exceeded by that of the paratyphoid cases, the reason being that the troops had frequently been inoculated against typhoid but not against paratyphoid.

Aetiology. Courtois-Suffit and Bourgeois emphasize the frequency and gravity of typhoid fever due to the consumption of oysters since the war. Of 118 cases of typhoid fever treated at the Hôpital Dubois, Paris, between July 1, 1919, and January 1, 1921, 35 were due to this cause. Of these 6, or 17 per cent., were fatal, and 25, or 71 per cent., had complications, whereas of 81 cases not due to this cause only 1 died and 8, or 9·8 per cent., had complications.

Carver records the case of a chronic female typhoid carrier who had an attack of typhoid fever in 1893, and between then and her death 21 years later, from malignant disease of the stomach and pancreas, infected at least 10 other persons who lodged with her. Treatment by various drugs as well as by an autogenous vaccine was ineffective. She suffered from numerous attacks of cholecystitis and biliary colic, which possibly caused a fresh discharge of bacilli into the intestine. At the autopsy gall-stones were present, and the typhoid bacillus was obtained from the bile and from the interior of a gall-stone.

Grant relates a case of laboratory infection which it is interesting to compare with that recently published by Hirschbruch and Forthmann (vide *Medical Science*, 1920, **2**, 3–4). A laboratory assistant, while working with a heavy suspension of living *B. typhosus*, sucked up about 0·5 c.cm. of the culture through the cotton plug into his mouth. He washed out his mouth thoroughly with 50 per cent. alcohol and was at once given 0·5 c.cm. of triple typhoid vaccine. He had already been inoculated with the same vaccine 14 months previously. Four days after infection he had a headache and malaise, but the temperature remained normal, and no further symptoms developed. On the twelfth day after infection *B. typhosus* was present in the stools, but by the fifteenth day it had disappeared, and was not found since. A blood-culture was negative. The case shows that in some cases at least typhoid inoculations will protect even against massive infection.

As a general rule, however, inoculation does not protect individuals against the injection of massive doses of typhoid bacilli. Cornwall and Crawford report an outbreak of 13 cases of typhoid fever which occurred in the course of a month in an American unit in France all the members of which had been inoculated against typhoid and paratyphoid A and B from six to sixteen months previously. Six died and twelve recovered. Other outbreaks of typhoid fever among inoculated American troops during the recent war, and ascribed to the ingestion of virulent organisms in massive and repeated doses, have been related by previous writers (vide *Medical Science*, 1919, **1**, 26).

An outbreak occurring in June of 28 cases of paratyphoid B infection due to eating cream tarts sold at a certain pastrycook's shop is reported by Lesné, Violle, and Langle. The tarts had been on a counter exposed to the sun for more than 24 hours, but had no unpleasant smell or taste. The symptoms were those of an ordinary acute gastro-enteritis. Although the cases were not isolated, no instance of contagion was observed. To prevent further epidemics of this kind the writers recommend an absolute prohibition of the sale of tarts containing raw cream in the summer, and suggest that permission to sell them at other seasons should be granted, provided the shop be kept very clean and free from animals, and the tarts be sold within twelve hours after being made.

Symptomatology. Remlinger records the case of a man, aged 30, in whom acute delirium with symptoms of rabies, such as hydrophobia, barking, and hyperacousia, was the first evidence of a rapidly fatal attack of typhoid fever. The autopsy showed an enlarged and diffluent spleen, much enlarged mesenteric glands, and swollen and ulcerated Peyer's patches. A pure culture of typhoid bacilli was obtained from the spleen and liver. Rabies was excluded by the fact that inoculation of rabbits and guinea-pigs with an emulsion of the spinal cord had no effect.

Delahet and Marcandier report a case of typhoid fever in a boy aged 16, in whom the initial symptoms of lethargy and ocular paresis suggested the diagnosis of lethargic encephalitis. Lumbar puncture gave issue to a clean sterile fluid with no increase of tension. Rapid improvement and final recovery took place after intrathecal injection of the patient's own serum. The true nature of the condition was discovered by a positive blood-culture and Widal's reaction.

Ickert reports a fatal case of typhoid fever with an *allergic temperature* in a woman aged 37, in whom death was due to broncho-pneumonia. The patient, who had had another attack of typhoid fever three years previously, presented an undulating type of temperature, such as has been described by Oeller and Meyer (vide *Medical Supplement*, 1919, **1**, 70) in inoculated persons who had contracted typhoid. As in the great majority of second attacks of typhoid fever on record in which symptoms of pneumonia or septicaemia predominated, intestinal symptoms in Ickert's case were absent during the second attack. The practical importance of such cases is, that in obscure disease associated with an undulating pyrexia the possibility of typhoid should be considered, as such an allergic type of fever may occur after a second infection or prophylactic inoculation.

Giovannini reports 11 cases of *relapse* in inoculated subjects which presented the following features: (1) mortality nil; (2) frequency about 5 per cent.; (3) generally mild character; (4) duration of about 9–12 days, in exceptional cases 15–27 days, especially in early relapses (first week of normal temperature); (5) usual date of appearance between fifteenth and twentieth day of apyrexia; (6) mode of defervescence usually by lysis. Giovannini maintains that relapses in typhoid fever are not due to dietetic errors as is generally supposed.

Bourges reports two cases of *typhoid septicaemia* in naval ratings aged 16 and 17 respectively, characterized by intermittent fever lasting from four to six weeks, accompanied by increase in size of the spleen and marked adynamia but with a complete absence of abdominal symptoms and of the other classical manifestations of typhoid fever. Malaria was excluded by the absence of haematozoa, and the diagnosis of typhoid was established by a positive blood-culture and Widal's reaction in both cases. The intermittent type of fever resembled that met with in meningococcal and gonococcal septicaemia, from which these cases differed in the absence of joint pains and of a polymorphous eruption. Lastly, whereas the general condition in meningococcal and gonococcal septicaemia shows hardly any disturbance and the spleen is little if at all enlarged, in these two cases there was decided enlargement of the spleen and pronounced adynamia.

The case reported by Rehberg in a soldier of typhoid septicaemia was characterized clinically by extremely severe septic symptoms. Bacteriological examination of the spleen showed typhoid bacilli, but contrary to expectation no evidence was found in the intestine to confirm the clinical and bacteriological diagnosis of typhoid fever. The case corresponds to Wolff-Eisner and Stadelmann's first group of typhoid septicaemia, which consists of cases presenting the clinical appearances of typhoid fever but differing from it in their morbid anatomy. In the present case the post-mortem appearances were those of general septicaemia.

Minet and Legrand remark that among the localized forms of typhoid infection the *cardiac form* deserves more attention than it has hitherto received. Although isolated cases have been reported in the literature by Nattan-Lavier, Farcy, Lesieur, Froment and Crémieu, and Mathews and Moir, a localized cardiac form of typhoid has not hitherto been described. The writers report two illustrative cases of septicaemia, in a woman aged 36 and a man aged 18, respectively, in which the typhoid origin was determined by culture and Widal's reaction, though there was a complete absence of any intestinal symptoms. In both cases the heart was affected, though in a very different manner in each patient. In the first case there was an involvement of the myocardium shown by adynamia, tachycardia, instability of the pulse, hypotension, embryocardia, and weakness of the heart-sounds. In the second case after a septicaemic stage the infection became localized in the pulmonary artery, giving rise to signs of pulmonary stenosis. Recovery took place in both cases.

Pollitzer states that as consultant to the Second Austro-Hungarian Army he had an opportunity of seeing about 20,000 cases of typhoid infections. Almost 70 per cent. of these were mild cases which showed hardly any other symptoms beyond fever of three or four weeks' duration and enlargement of the spleen. About one in every thousand, however, independently of the season of the year and other circumstances, differed from the other cases by presenting considerable enlargement of the liver. Pollitzer regards this enlargement as a manifestation of ambulatory typhoid associated with juvenile hypotonus, and suggests the term 'cardio-typhoid', on the analogy of nephro-, pleuro-, and pneumo-typhoid, as applicable to such cases.

Rist records the case of a man, aged 30, who developed paratyphoid A after being subject to attacks of *paroxysmal tachycardia* for several years. During the course of the fever he had four attacks of tachycardia in sixteen days, the first lasting 3½ days, the second 2½ days, and the last two about 24 hours. Each of the paroxysms coincided with a sudden fall of the temperature, which dropped the first time from 104·4 to 98·4 and the second time from 104·4 to 96·8. During the last two attacks the fall of temperature was less striking, as it occurred during defervescence, when the fever was showing a natural tendency to subside. Throughout the duration of the attack the temperature remained normal or nearly so, and gradually became febrile again at the end of the paroxysm. During the attack the pulse-rate was 180–200 with a very definite foetal rhythm, whereas before the attack it varied from 76 to 88, as is the rule in typhoid fever.

A case of *arterial hypertension* in marked contrast with the low blood-pressure which is the rule in typhoid fever is reported by Lemierre and Piédelièvre. The patient was a man, aged 32, who in the third week of a moderate attack of typhoid fever suddenly developed polyuria, the amount of urine rising from $1\frac{1}{2}$ to $3\frac{1}{2}$ litres in the 24 hours. The maximum blood-pressure as measured by Pachon's sphygmomanometer was 21, and the minimum pressure 11. Epistaxis followed by intestinal haemorrhage occurred on the afternoon of the same day, and death took place from pulmonary complications. The writers state that Teissier, in 1900, and subsequently Crile, Carrière and Dancourt, Huchard and Amblard, Barach, Olmer and Roger Voisin, showed that a sudden rise of blood-pressure in typhoid fever is a bad prognostic. Hypertension does not herald intestinal haemorrhage only, but may be the prodromal sign of perforation, pulmonary complications, or delirium. In the present case the hypertension was accompanied by two symptoms not hitherto described in this connexion, viz. polyuria and epistaxis.

Bunn reports a hitherto undescribed complication of typhoid fever, viz. *thrombosis of the posterior orbital veins* giving rise to oedema of the left eyelid and proptosis. In 36 hours the oedema disappeared and the eyeball returned to its normal position with no impairment of vision.

Compagnon remarks that *pleurisy* is far from rare in typhoid fever, and that apart from tuberculous effusions occurring in convalescence the causal agent is usually the typhoid bacillus, at least in the case of serous effusions. In empyema, whether it be primary or secondary to a pulmonary lesion, several organisms are concerned, the pneumococcus (Netter, Courmont and Martin), streptococcus, staphylococcus (Remlinger, Triboulet), *B. coli* (Macaigne and Théry) being found either alone or in association with the typhoid bacillus. Compagnon records a fatal case in a man, aged 41, of empyema following a severe attack of typhoid complicated by broncho-pneumonia and due to strictly anaerobic organisms, viz. *B. fragilis* and an anaerobic streptococcus.

According to Lemierre and Deschamps the *pulmonary localizations* of the typhoid and paratyphoid bacilli may be manifested clinically by symptoms identical with those of miliary tuberculosis or caseous phthisis. Even when the existence of typhoid or paratyphoid fever is confirmed by blood-culture or Widal's reaction, the development of pulmonary symptoms may suggest the presence of acute tuberculosis. In spite of what is stated in some text-books, the occurrence of acute tuberculosis in typhoid fever is exceptional, Bernard having found tuberculous lesions in only 2 per cent. of his typhoid cases. The onset of pulmonary symptoms in a case of enteric fever confirmed by laboratory examination should first suggest a localization of the typhoid or paratyphoid bacillus rather than of a superadded tuberculous infection. Laboratory tests are essential for establishing a rapid diagnosis in such cases. Tuberculosis can be excluded by the absence of the tubercle bacillus, or, better still, by the presence of typhoid or paratyphoid bacilli in the sputum, and by a cytological examination of the pleural effusion, which shows endothelial and polymorphonuclear cells in contrast with the lymphocytosis of tuberculous effusions.

Giosetti maintains that *intestinal complications* are rare in children who contract typhoid, but are more serious than in the adult, the incidence being 1–2 per cent. with a mortality of 67–92 per cent. He records two cases of intestinal perforation in children, one being a girl, aged 14, in whom operation was successful, and the other a boy, aged 6, in whom a typhoid ulcer in Meckel's diverticulum was found *post mortem* to have given rise to a localized adhesive peritonitis. The state of collapse on admission to hospital and the co-existence of endocarditis had contra-indicated any operation in this case.

According to Svartz and Hanson, who record a fatal case in a woman, aged 26, in whom death was due to broncho-pneumonia 12 days after laparotomy, there are about 40–50 cases on record of peritonitis due to propagation of the inflammation through the intestinal wall without perforation. A little more than a third are examples of fibrinous peritonitis, two are cases of purulent peritonitis, and in the remainder the peritonitis was sero-fibrinous. About 25 per cent. of the patients recovered after operation. In four cases typhoid bacilli were found in the peritoneal exudation.

Bazán records a case of a mild attack of typhoid in a girl aged 5, complicated by *torticollis* due to myositis of the trapezius, which ended in sclerosis. The child was predisposed to this complication by the fact that a year previously she had had an attack of torticollis of eight days' duration, and was also the subject of hereditary syphilis.

Weil maintains that of the different varieties of enteric fever typhoid is almost exclusively responsible for *osteo-arthropathies.* Of 18 cases observed by him only two were due to paratyphoid B and none to paratyphoid A. The condition is most likely to occur after long and severe attacks of typhoid fever, and consequently in non-inoculated subjects. 14 of the 18 cases had not been inoculated at all, two had been inoculated incompletely, and only two had had four injections. In the adult the osteo-arthropathy affects the ribs and costal cartilages almost exclusively, and only rarely the vertebral column or the long bones. In the adolescent it affects chiefly the long bones, in which it involves the epiphyses at the elbow in the upper limb and the trochanters and malleoli in the lower extremity. The nature of the bone lesion can be detected by study of the agglutination, whereby not only can typhoid and paratyphoid osteitis be distinguished from other forms of osteitis but osteitis due to *B. typhosus* can be distinguished from that due to *B. paratyphosus* A or B. In true typhoid osteitis the agglutination titre is very high, whereas in post-typhoid osteitis due to other causes than typhoid it is nil or very low.

Castro, of Montevideo, who records a case of spontaneous dislocation of the hip due to typhoid monarthritis in a boy aged 13, states that 90 per cent. of the dislocations in typhoid fever occur at the hip-joint. According to Keen, who collected 43 cases of spontaneous dislocation in typhoid fever, 40 of which occurred in the hip, two in the shoulder, and one in the knee, the dislocation is due to an infective osteitis, which by enlarging the head of the femur forces it out of the acetabulum. Other authorities on the other hand, such as Broca, maintain that the attitude of flexion and adduction during arthritis causes pressure of the head of the femur against the posterior part of the capsule, which gives way.

Although *abscesses* due to *B. typhosus* have been reported as occurring in a number of different situations (vide *Medical Science*, 1920, **3**, 206–7), no previous example of its location in a mammary abscess has been reported. Dyke relates the case of a woman who, after suffering from a severe but undiagnosed illness, developed an abscess of the breast without any apparent association with the underlying bone. A pure culture of *B. typhosus* was obtained from the pus, and the same organism was also found in the stools, although the serum showed an absence of agglutinins.

Lesné reports a case of paratyphoid B fever in a man aged 25 complicated on the sixteenth day by *suppurative meningitis.* A pure culture of the paratyphoid B bacillus was obtained from the cerebrospinal fluid. Lumbar puncture was performed every other day, and was followed on three occasions by intrathecal injection of 5 c.cm. of 1 per cent. solution of collargol. The fourth lumbar puncture performed ten days after the first showed a clear sterile fluid with only a few lymphocytes. Although Sacquépée, Boidin, Laroche, and Lacaplain have reported instances of meningeal syndromes with a clear and sterile cerebrospinal fluid in paratyphoid B fever, only one previous case of suppurative paratyphoid B meningitis, recorded by Tollemer and Weissenbach, has been published.

Bossert, of the Breslau University Children's Clinic, records seven cases of severe paratyphoid fever in children, associated with characteristic symptoms of *tetany*. Mechanical and electrical hyperexcitability was well marked, but no attacks of laryngospasm were observed. It could not be determined how the endotoxin acted, whether by attacking the anterior cornual cells or the parathyroids directly, or in some other way. Bossert suggests that the attacks of carpopedal spasm and mechanical hyperexcitability following febrile diarrhoea in infants, as described by writers in the prebacteriological era, were really due to paratyphoid.

Inoculation. In his report on antityphoid and antiparatyphoid inoculation in the Royal Navy for 1919–20 Bassett-Smith states that from October 1, 1919, to September 30, 1920, 13,343 men were inoculated, 4,045 being given one inoculation and 9,298 two inoculations. During the year the total number of enteric cases was 66, the incidence being as follows: 53 typhoid, 4 paratyphoid A, 7 paratyphoid B, and 2 paratyphoid C. There were four deaths, two of which were from typhoid in men inoculated twice, one from paratyphoid B in a man who had not been inoculated, and one from paratyphoid C after inoculation with T.A.B. vaccine. As cases of irregular enteric which had been traced to infection with paratyphoid C had been noted for the Eastern area, this organism was added to the vaccine for the Mediterranean and Middle East, the new vaccine being named T.A.B.C.

Kramer remarks that preventive inoculation against enteric fever has considerably increased the difficulties of diagnosing the disease in inoculated individuals. He records two cases in which the temperature was irregular, and the Widal reaction did not become positive until a late stage or shortly before their discharge from hospital. In one case the temperature resembled that of malaria, although examination of the blood was negative, and in the other it assumed an undulating type with an interval of four to six days between the crests of the waves, while in the intervals it was normal or subfebrile, the patient's general condition being correspondingly affected.

The advisability of inoculating the civilian population, as was done in Flanders in 1915 and 1916 (vide *Medical Science*, 1919, **1**, 25–6), is urged by Chauffard, Achard, Sergent, and Vincent, as well as by a commission appointed by the Académie de Médecine, composed of Bernard, Cazeneuve, Widal, Roux, Vincent, Calmette, and Chauffard. Chauffard suggests that the first inoculation should take place at 15 years of age, the second at 18, and the third at 21. Vincent specially advocates inoculation of the civilian population under the following circumstances: (1) In districts where typhoid fever is endemo-epidemic. (2) In families in which one or more persons are suffering from the disease. (3) When the history and *a fortiori* bacteriological examination show the existence of carriers among healthy persons. In all such cases inoculation should be performed without delay or it may be too late. But even in the incubation stage it may be of use by attenuating the infection, and it may even prevent it altogether, if it is performed during the early part of the incubation stage. The commission appointed by the Académie de Médecine, besides recommending that in case of an epidemic the whole population should be inoculated, children and old persons included, suggest that every notification of a case of typhoid fever should be accompanied by a note as to previous inoculation.

After alluding to the various sequelae of antityphoid inoculation, such as albuminuric retinitis in subjects of Bright's disease (vide *Medical Science*, 1919, **1**, 30), sudden death from oedema of the glottis in status lymphaticus (*ibid.*, 31), Landry's paralysis (*ibid.*, 1920, **2**, 8), cortical thrombosis, &c., Bury reports a case presenting symptoms of tabes in a man aged 36, which developed a few hours after a second injection of antityphoid vaccine. Ataxia, hypotonus, sluggish knee-jerks, and unequal pupils were present, but the Wassermann reaction was negative in the blood and cerebrospinal fluid.

According to Bourges (2) pulmonary tuberculosis is a formal contra-indication to antityphoid inoculation, as is shown by the numerous cases in which dormant tuberculosis has been roused into activity as the result of inoculation in subjects with old pulmonary lesions. Bourges records a fatal case of miliary tuberculosis of insidious and apyrexial course following inoculation in a naval rating aged 16, the subject of pulmonary tuberculosis.

Treatment. Galata treated 303 cases of typhoid fever by *intragluteal injections of calomel*, the doses being 10 cgm. for adults, 5 cgm. for adolescents, and a proportionally smaller dose for children. The injections were given on alternate days. If the fever persisted two days after the fourth injection, a fifth was given, and in obstinate cases a sixth. The preparation used consisted of calomel, guaiacol, camphor, āā 0·10 gm., vaseline 1 c.cm. The results of treatment were as follows: (1) Comparatively mild course of the disease after the second injection. (2) Rapid and considerable shortening of the febrile stage, a normal temperature being reached between the third and fourth injection or a few days after the fourth. (3) Complete local, renal, and general tolerance of the drug apart from a few cases of stomatitis. (4) The best results were obtained in early cases, and in those with an absence of organic lesions. The mortality among 234 cases was 1·7 per cent., or four deaths, three of which were due to bronchopneumonia, which was present before the treatment was started.

During a severe epidemic of typhoid fever in Rome from 1912-14 Cataldi observed that, whereas among the hundreds of injections of quinine given to malarial patients, there were only two or three examples of suppuration, which were rather of a chemical than bacterial character; in the cases of typhoid fever a large number of the quinine injections suppurated with the formation of laudable pus, the suppuration almost always coinciding with improvement which ended in recovery. During the autumn and winter of 1920–1 a fresh outbreak of typhoid fever occurred, when Cataldi determined to employ treatment by *fixation abscess* produced by subcutaneous injection of 1 or 2 c.cm. of oil of turpentine. He records four cases of severe typhoid—two in adults and two in children—in which this treatment was successful.

As *injections of milk* have been recommended in a variety of conditions, Nello's unfavourable experience is instructive. 21 cases of enteric fever, consisting of 16 cases of typhoid, 3 of paratyphoid A, and 2 of paratyphoid B, were treated by intragluteal injections of sterilized milk in doses of 10 c.cm., the injections being repeated four or five times at intervals of two to four days. In 7 cases the first injection was given in the first week of the disease, and in 14 cases in the second week. The injections almost always caused severe local pain, accompanied by a sharp rise of temperature, without shortening the course of the disease or having any beneficial effect on any of the symptoms.

The value of Rodet's *serum* (vide *Medical Science*, 1919, **1**, 31; 1920, **2**, 209) is confirmed by Étienne, of Nancy, who states that when it is employed between the eighth and tenth day, apart from any other treatment except cardiac tonics, the disease is almost invariably aborted. The effect of the serum on the temperature is shown in one of three ways: viz. by (1) a sudden drop; (2) a fall by lysis; (3) an amphibolic stage. When the serum is employed later it may also have an abortive effect, but this is not the rule. When it is employed before the eighth day the results are unfavourable, or at least the benefit is much less definite. A few cases of serum rash were observed, but no instance of any really bad effects from the serum was observed.

Le Blaye (1) reports seven cases of typhoid fever treated by Vincent's serum, which is both antitoxic and bactericidal. It was found to be of value in severe cases, and often caused a very rapid fall of temperature. Apart from the ordinary serum manifestations it did not give rise to any complications.

Le Blaye (2) also reports 21 cases of typhoid fever treated by *vaccines* given by mouth. The vaccine was given in the patients' ptisan without their knowledge, and did not produce any digestive disturbance, even in severe attacks. It was absolutely harmless, and there was no contra-indication to its use. Le Blaye claims that his method contributed in a great extent to the favourable results obtained.

Dufour, Debray, and Guyard relate a case of typhoid spondylitis of the second lumbar vertebra in a woman aged 42, successfully treated by five injections of Vincent's T.A.B. vaccine after other methods had failed. Three other cases of typhoid spine cured by T.A.B. vaccine had been previously recorded by Dufour.

From observation of 30 cases—20 adults and 10 children—Korbsch found that early autovaccine therapy of typhoid with intramuscular injections of 250 to a thousand millions at intervals of four days was a safe procedure, caused few symptoms, and usually made the disease take a short and favourable course. A high continued fever was usually converted by the first injection into a remittent or intermittent one. Complications, recrudescences, and relapses were usually avoided, and convalescence was rapid. Only one of the 30 cases died, but he did not come under treatment until the third week.

Henes, jun., who records seven illustrative cases, confirms the observations of Nichols, Simmons, and Stimmel as to the value of the *surgical treatment of typhoid carriers* (*Medical Science*, 1920, **2**, 10–11), and maintains that cholecystectomy with complete excision of the cystic duct will cure the great majority of such cases. The operation is not required until six months after the onset of the disease.

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J. D. R.

DISEASES OF DUCTLESS GLANDS

Thyroid. S. Levin examined 1,783 unselected persons aged from birth to sixty-one years living in the Great Lakes goitre belt, and found that 1,146 had some enlargement of the thyroid, which was due in 682 to simple goitre, in 420 to adenoma and cystoma, and in 42 to colloid. The incidence curve showed that goitres increase in both sexes during puberty, dropping to a small degree after the full growth of the individual is attained. The curve is maintained in the female for the child-bearing period, dropping at about 38 or 40 years, and rising again at the menopause. In the male the curve gradually drops till 35 or 40, when there is a small rise. Simple goitres maintain the high percentage till 35, and the adenoma and cystoma sustain the height of the incidence curve after that age.

Writers are still far from unanimous as to which gland or glands of internal secretion are responsible for Graves's disease. In a discussion on the medical and surgical treatment of Graves's disease at the Royal Society of Medicine, Williams contended that Graves's disease was not only not a hyperthyroidism but was not a disease of the thyroid gland at all. He stated that the most outstanding feature of the complaint, namely, exophthalmos and cardiac troubles were due to the implication of other glands, the exophthalmos being due to adrenal excess and the cardiac symptom to enlargement of the thymus. He considered that this enlargement, which occurred in 85 per cent. of the cases, caused not only the cardiac symptoms by pressure on the base of the heart and great vessels, but also many of the nervous symptoms by pressure on the vagus, sympathetic, and phrenic, as well as mental symptoms by interfering with drainage from the brain. He regarded Graves's disease as due to a toxaemia in which all the members of the endocrine hierarchy were involved. The only way of treating the disease, in his opinion, was by discovering the source of the toxin and eliminating it. In a large percentage of cases the toxin was gastro-intestinal, and could be successfully dealt with only by dieting and, if necessary, intestinal antiseptics.

Swiecicki, of Posen, is inclined to regard Graves's disease as due to hyperactivity of the suprarenals, the vasomotor and secretory symptoms, including tachycardia, tremor, and exophthalmos, being caused by an increase of adrenalin secretion. He therefore recommends that treatment should aim at diminishing the production of adrenalin by administration of oil of sesame and hypotensive measures, including mild hydrotherapy, rest, and residence in a mountainous climate.

On the other hand, Rautmann, of the Freiburg University Medical Clinic, regards the tachycardia, exophthalmos, and morbid excitability of the whole nervous system, and increase of metabolism, as due to overactivity of the thyroid. Although he is convinced that the thyroid plays a leading part in the pathogenesis, he admits that Graves's disease may sometimes be neurogenic, i. e. caused by an abnormal stimulation of the nervous system, the over-action of the thyroid being secondary. Moreover, owing to the intimate relationship of the ductless glands with one another, he thinks it possible that involvement of another endocrine organ such as the thymus may be the primary cause of the development of Graves's disease.

According to G. A. Friedman (1), of New York, the hypophysis shows histological changes in Graves's disease similar to those in hyperpituitarism and in myxoedema to those in hypopituitarism. There is therefore a certain degree of hypophyseal hyperactivity in hyperthyroidism and of hypoactivity of the pituitary in hypothyroidism. Consequently pituitary products are contra-indicated in exophthalmic goitre and indicated as well as thyroid extract in myxoedema.

Elsewhere Friedman (2) points out that some of the symptoms of Addison's disease, such as emaciation, asthenia, and hyperpigmentation, which are chiefly due to various degrees of adrenal insufficiency, appear in a lesser degree in subjects of Graves's disease.

Owing to the mild degree of cortical hypofunction in hyperthyroidism these symptoms are not as frequent or as pronounced as in Addison's disease. Hyperpigmentation in Addison's disease as well as in Graves's disease is due to the same cause, viz. increased retention of uric acid in the blood on account of adrenal cortex insufficiency. The gain in weight and absence of true asthenia in myxoedema is attributed by Friedman to hyperfunction of the cortex. Abnormal pigmentation of the skin is absent in myxoedema because the elimination of uric acid is increased, and the rest which is not eliminated the hyperfunctioning cortex is able to oxidize in its tissue.

In a critical review of the emotional origin of Graves's disease, Roussy and Cornil state that only seven or eight cases which have been published in France, and a few in other countries, can be regarded as supporting this theory. In none of the cases could they find that a sudden emotion had given rise to the disease. Several other neurologists, such as Barré, Crouzon, Lépine, and Lhermitte, who had been in charge of special centres during the war, had also declared that they had never seen a typical case of exophthalmic goitre following a war emotion. Roussy and Cornil therefore regard it as a mistake to insist on making emotion responsible for a syndrome in which the emotional state represents the effect rather than the cause.

Moore, who reports two illustrative cases, considers that the increase of orbital fat is the usual cause of the exophthalmos in Graves's disease, and that at present there is no satisfactory evidence that there is any other cause for it, such as irritation of the sympathetic nerve producing contraction of unstriped muscle in the orbit or engorgement of the orbit with blood. He regards the limitations of the eye-movements frequently present in Graves's disease as produced mechanically by pushing forward of the eye, and not by nerve or muscle defect, and suggests that oedema of the muscles contributes to this restriction of movement.

According to Sattler, of Leipzig, the occurrence of retrobulbar neuritis in Graves's disease is very rare, and has not hitherto been described as an initial symptom. He records a case of Graves's disease in which a diminution of visual acuity was the first thing which induced the patient to seek medical advice. All other possible causes of the neuritis could be excluded, and resection of the thyroid simultaneously benefited the retrobulbar neuritis, exophthalmos, and other symptoms of Graves's disease. A few other cases have been reported in which on improvement of Graves's disease the optic neuritis subsided. There are also cases on record of misuse of thyroid tablets being followed by retrobulbar neuritis, and finally Sattler found that experimental administration of thyroid tablets to animals produced a disease of the optic nerve resembling toxic amblyopia.

Smit records two cases of toxic thyroiditis due to syphilis with all the symptoms of Graves's disease in women aged 34 and 52 respectively, who were both completely cured by a course of antisyphilitic treatment.

A case of malignant tumour of the thyroid with metastases in the bones is reported by Tixier and Duval. As is the rule in such cases, as shown by Lenormant, the picture of Graves's disease was incomplete, tachycardia and tremor being present and exophthalmos absent.

Frantz, of New York, describes a case of hyperthyroidism in a girl which appeared at the age of 1½ years, and may have existed even before that time. At the age of 9 years she had exophthalmos, a visible and palpable thyroid, tachycardia, and a mental age of 12 years. The condition was probably congenital, as the parents had lived in a goitrous district, the mother was the subject of hyperthyroidism and the child was mentally precocious.

Fleischner, of the First Medical Clinic in Vienna, reports a case of Graves's disease in a woman aged 41, with a cutaneous oedema of the lower part of the body resembling sclerodermia, in whom irradiation of the ovaries was followed by amenorrhoea and aggravation of the general condition. He alludes to two other cases on record in which X-ray treatment had a similar effect.

According to Boothby (1) adenoma with hyperthyroidism resembles exophthalmic goitre in being characterized by an increased basal metabolic rate, but differs from it in its clinical course. Moreover, exophthalmic goitre has certain peculiar symptoms, such as exophthalmos, thrills and bruit, tendency to gastro-intestinal crises, and a peculiar type of nervousness.

Apart from differences in the onset, duration, course, and outcome, the operative procedure in the two diseases is different. In adenoma with hyperthyroidism the operation is directed to removal of the tumour, while in exophthalmic goitre the object of the operation is to reduce the overactivity of the diffuse parenchymatous hypertrophied thyroid by successive steps, viz. first, hot-water injections, secondly, one or more ligations, and thirdly, one or more partial thyroidectomies.

Numerous writers, such as Boothby (1), Frazier and Adler, Janney and Henderson, Mayo, Mosenthal and Marks, Sanger and Bauman, Sturgis and Tompkins, C. M. and D. Wilson, emphasize the importance of the determination of the basal metabolism in the diagnosis and treatment of hyperthyroidism and hypothyroidism. According to Frazier and Adler, estimations of basal metabolism are of value in the following ways: (1) Positive. In eliminating those cases which will not be benefited and might be made worse by operation. (2) Supplemental. (*a*) In offering confirmatory evidence of the degree of toxicity; (*b*) in offering a quantitative rather than a qualitative index in diagnosis, prognosis, and treatment. (3) Problematical. It may be possible to determine by the metabolic rate how much thyroid tissue may be removed. Reduction of the metabolic rates to points well below that of the normal range (−10) should imply that too much secreting substance has been removed. Mayo points out that many psychoneurotic patients would be placed in the group of exophthalmic goitre cases on the basis of the epinephrin test, whereas a failure of diagnosis is almost impossible if the basal metabolic rate is taken into consideration with the other general symptoms. C. M. and D. Wilson consider that estimations of the basal metabolic rate amply justify the time spent upon them, as they mark off toxic from non-toxic goitre, establish or refute suspicions of hyper- or hypothyroidism, and furnish a graphic method of the results that follow the treatment of these conditions. In a study of 496 basal metabolism determinations on 154 patients with hyperthyroidism, Sturgis and Tompkins found tachycardia of 90 or more to the minute associated with a basal metabolism of +15 per cent. or more in all but 16 per cent. In 70 instances where the metabolism fell to normal there was a simultaneous fall in pulse-rate in 78 per cent. to below 90. In 52 patients in whom a number of metabolism determinations were made the pulse-rate gave an accurate idea of the course of the disease as compared to the basal metabolism in 85 per cent. In a series of 106 hospital patients with various diagnoses and normal basal metabolism only 5 had a heart-rate of 90 or more to the minute. There was in general an interrelationship between the pulse-rate and metabolism where a group of individuals was considered, in other words, an extreme degree of tachycardia suggested a greatly increased metabolism, while a slight tachycardia usually indicated a slight or moderate increase. The fact that a pulse-rate below 90 per minute is seldom and below 80 per minute is rarely associated with an increase in metabolism is regarded by Sturgis and Tompkins as of great practical importance in the recognition of a large group of nervous patients who have symptoms similar to those occurring in hyperthyroidism (*vide* also *Medical Science*, 1920, **2**, 126–7).

Bram, of Philadelphia, recommends the following quinine test which he has employed for three years in a series of 160 cases, 67 of which proved to be instances of thyroid toxaemia. The patient is given a dozen capsules each containing 10 grains of the neutral hydrobromide of quinine, with instructions to take one capsule four times daily, followed by an ample supply of lukewarm water, one or two hours after food and at bedtime. When 30–50 grains have been taken by persons whose thyroid function is not excessive, there develops a sense of fullness in the head, impaired hearing with tinnitus, and often dizziness and headache. Persons with a susceptibility or idiosyncrasy for quinine will experience these symptoms after the first or second capsule, while those who are specially tolerant will not complain till 60–100 grains have been taken. In the case of a hyperactive thyroid no symptoms develop from daily administration of quinine hydrobromide even when it is given daily for weeks or months. Bram regards this test as superior to any other on account of its simplicity and harmlessness. Though there may be a 5–10 per cent. error in its use, it is specially commendable in that its interpretation does not depend upon an aggravation of the symptoms of hyperthyroidism, but in many instances it causes an improvement in the symptoms of Graves's disease.

Goodpasture, of Boston, records two fatal cases of hyperthyroidism in which the most prominent clinical manifestations were cardiac weakness and auricular fibrillation, and *post mortem* myocardial necrosis was found in both, being very extensive and diffuse in one and limited and focal in the other. He suggests that the myocardium in these cases was abnormally susceptible to injury such as may have been caused by an undiscovered terminal infection or by a sudden functional strain.

Meissner (1), of the Breslau University Medical Policlinic, records three cases of myxoedema with a description of their cardiac condition. At the height of the disease the pulse was remarkably slow in all three patients, being only 50–58. As improvement took place the pulse-rate returned to the normal. The blood-pressure and size of the heart differed considerably in each case. In the severest and most chronic cases there was considerable dilatation of the right and left heart, which, as Zadek as shown, is characteristic of myxoedema (vide *Medical Science*, 1920, **2**, 131). Under treatment by thyroidin the dilatation subsided. In the second case the cardiac condition was complicated by the presence of chronic nephritis, and the size of the heart was not affected by thyroidin. In the third case the absence of any cardiac change was due to the acute course, complete recovery occurring within eight weeks under thyroidin treatment.

Hardenbergh reports a case of myxoedema which in the long duration of treatment resembles that recently reported by Murray (vide *Medical Science*, 1920, **3**, 216). In 1882 a woman aged 26 began to develop symptoms of hypothyroidism. Thyroid treatment was not started till twelve years later, at the age of 38. Rapid recovery took place, and was maintained for 26 years, during which time thyroid feeding was continued, the patient being in good health at the time of publication.

A fatal case of myxoedema with pluriglandular insufficiency, in which death was due to softening of the left cerebellar hemisphere, is reported by Meissner (2). The autopsy showed marked atrophy of the ovaries and great increase of pigmentation in the suprarenals and hypophysis as well as atrophy of the thyroid.

Kuhlmann, of the Greifswald University Medical Clinic, records two cases in women, aged 44 and 27 respectively, both of whom showed some of the features of myxoedema, though the complete clinical picture was not well developed in either. A series of tests, including sensitiveness to adrenalin, pilocarpine, and homatropine, resistance tests with carbohydrates and normal saline, showed that one case was a rudimentary myxoedema and the other an example of ovarian insufficiency. Owing to the therapeutical importance of an early diagnosis in such conditions, Kuhlmann emphasizes the importance of employing these simple tests.

Seymour, of Boston, reports two cases of women who developed myxoedema after X-ray treatment for Graves's disease. Both recovered under treatment with thyroid extract.

Simmonds, of Frankfort, records two cases of myoclonus in women aged 22 and 28, in whom the condition was cured by thyroid gland tablets, which were given because, in addition to the myoclonus, symptoms were present in both cases which indicated thyroid insufficiency. The theory that myoclonus is due to auto-intoxication especially affecting the thyroid is thus confirmed by these two cases.

Parathyroids. According to Boothby (2), of the Mayo Clinic, the only definite clinical entity which has been proved experimentally to be of parathyroid origin is the tetany occasionally seen after operations on the thyroid. In these conditions calcium in large doses usually ameliorates the symptoms. He remarks that the experimental evidence pointing to the parathyroids as the primary cause of idiopathic tetany unassociated with operations on the thyroid is very limited.

Roth reports a case of tetany in a woman aged 32, in the sixth month of her fifth pregnancy, in whom a parathyroid which had been removed from another patient during a thyroidectomy had been transplanted into the right rectus sheath under local anaesthesia. The first three days after the operation no attacks occurred, and then only three mild ones during the next twelve days. Subsequently there were no further attacks during her pregnancy. The puerperium was normal, and the mother was able to suckle her child.

Under the title of 'an undescribed condition of infancy and its treatment', Clark, of Glasgow, describes two cases in children aged 15 months and 2½ years whose principal symptoms were idiocy, depression, fibrillary twitchings in the muscles, jerking movements in the limbs, convulsions, and inability to balance. Considerable improvement took place in both cases under treatment with parathyroid gland tablets. The symptoms were very similar to those observed by Paton and Findlay after thyro-parathyroidectomy in animals, so that Clark's cases were probably examples of parathyroid tetany.

Thymus. In an article on the relation of the persistent thymus gland to criminology, Morris, professor of anatomy in the West Virginia Medical School, states that out of 192 bodies of persons aged from 17 to 86, examined in the anatomical laboratory, 22 showed persistent thymus glands. 20 of these glands were taken from the bodies of criminals sent by the State Penitentiary, all of whom, except one who had been convicted of rape, were first or second degree murderers. The gland weighed from 5 to 29 grammes, and histologically showed normal thymus structure. Morris concludes that the persistent thymus is in some way accountable for the mental state that caused these men to be criminals.

According to Browning the existence of thymic epilepsy is shown by (*a*) presence of thymism, (*b*) absence of other recognizable causes of epilepsy, such as heredity, degeneracy, and morbid processes not of thymic origin, (*c*) peculiarities in the course of the epilepsy itself. Browning records an illustrative case in a man aged 25 with a persistent thymus, in whom the onset of epilepsy occurred at 21 without any mental defect. There was no evidence of syphilis. The seizures occurred only at long intervals, unlike those of thyroid epilepsy.

Harvier reports a case of lymphosarcoma of the thymus in a woman aged 25, characterized by a syndrome indicating compression of the superior vena cava, and consisting in cyanosis of the face, oedema of the front of the thorax, extraordinary development of the collateral venous circulation from the face to the pubes, as well as in a continuous cough, with attacks of suffocation and intermittent pain in the left shoulder and arm. Physical examination showed retrosternal and left subclavian dullness, left pleural effusion, no cardiac symptoms except permanent tachycardia, and no signs of bronchial compression. Death took place eight months after the first symptom, and the autopsy confirmed the diagnosis of a large tumour of a sarcomatous nature occupying the region of the thymus and involving secondarily the lungs, heart, diaphragm, liver, and kidneys.

Suprarenals. Eidelsberg, of New York, reports a case of Addison's disease which confirms Osler's statement that the cases in which the bronzing is slight or absent run an unusually rapid course. The patient was a man aged 30, in whom the onset was sudden, and the typical symptoms of the disease were present for only 16 days. The predominant features of Addison's syndrome, namely, asthenia, irritability of the stomach, and change of colour of the skin, were present, together with a remarkably low blood-pressure (systolic 70–80 mm. Hg, diastolic 50–60), but the bronzing of the skin was represented only by a general 'tan', and only a suggestion of buccal pigmentation existed. The diagnosis was confirmed by the autopsy, which showed an extensive tuberculosis of the suprarenals.

Sézary remarks that the sympathetic system has long been regarded as responsible for the pigmentation found in Addison's disease, but can find no adequate evidence for this hypothesis. On the other hand, he marshals many facts which tend to show that this pigmentation is due to an increase of the normal melanin-forming functions of the skin and that this increased function is brought about by various endocrine disorders. He does not suggest that any one of the endocrine glands is alone to blame.

Kay and Brock investigated the white line regarded by Sergent as due to hypo-adrenia in 255 cases comprising all types of diseases and a series of normal persons, and came to the conclusion that it was a local vasomotor reflex resident in the skin, bearing no direct relationship to adrenal activity. Their reasons for this conclusion were (*a*) its independence of blood-pressure, acute fatigue, and other signs of hypo-adrenia; (*b*) its frequent occurrence in normal persons and in a variety of diseases unassociated with hypo-adrenia; (*c*) its reappearance in spite of other general effects of adrenalin administered subcutaneously, such as tremor, throbbing of vessels, cardiac palpitation, heightened blood-pressure, &c.; (*d*) its peculiar association with scarlet fever.

Freudemann reports a case of suprarenal apoplexy in a soldier aged 20, secondary to verrucose endocarditis due to gas poisoning. The symptoms consisted of intermittent colic of considerable severity with a rise of temperature without vomiting or obstruction to the passage of flatus. The autopsy showed verrucose endocarditis, embolism of a branch of the pulmonary artery, apoplexy of both suprarenals, and an area of softening in the left temporal and parietal lobes.

According to Deglos, who records an illustrative case in a woman aged 28, rapid and complete cessation of both suprarenals with transformation of one of them into a large cold abscess is rare, especially when most of the symptoms of Addison's disease are absent. Deglos's case took the form of an attenuated septicaemia, with a temperature which suggested typhoid or paratyphoid fever. Death took place suddenly. In addition to the suprarenal lesions the autopsy showed marked hypoplasia of the ovaries and slight thyroid hypoplasia. Deglos suggests that in an infective process in which several blood cultures do not explain the cause of the condition, the possibility of a cold suprarenal abscess should be considered, when very pronounced hypotension is associated with extreme prostration without the presence of other signs of chronic suprarenalitis.

Hypophysis. From the examination of five anencephalic monsters, Browne has come to the conclusion that the characteristic physical signs of anencephaly, apart from the absence of the brain and cranial vault, are connected with absence of the pituitary gland. These characteristic physical signs are as follows: (1) Maldevelopment of the basis cranii; (2) protruding eyeballs; (3) protruding tongue; (4) aquilinity of nose; (5) large amount of cutaneous fat; (6) hyperplasia of the thymus; (7) small or absent suprarenal gland; (8) hypoplasia of the genital organs; (9) stunted growth of the trunk and limbs. Browne maintains that the internal secretions of the mother play no part, or at least a very minor one, in the development of the foetus, as they seem to have no effect in compensating for the secretions that are wanting in anencephaly. It is evident, also, that the endocrine glands of the foetus play an extremely important part in its development *in utero*.

Reye remarks that in addition to the two well-known types of pituitary disease, viz. acromegaly and dystrophia adiposo-genitalis, there is a third type which has been described by Simmonds, of Hamburg, under the name of cachexia of pituitary origin. It is characterized by severe cachexia with atrophy of all the organs, loss of teeth, eyebrows, eyelashes, axillary and pubic hair, as well as by psychical disturbance. This form of cachexia is caused by necrosis of the anterior lobe of the hypophysis, resulting from embolic processes occurring in the puerperium, and less frequently by malignant tumours or tuberculosis. Reye reports a case in a woman aged 50 in whom the condition was due to acquired syphilis and was cured by antisyphilitic treatment. This is the first case on record in which pituitary cachexia was due to syphilis. In the seven other published cases of syphilis of the hypophysis (in six congenital syphilis and in one acquired syphilis) the clinical picture was that of dystrophia adiposo-genitalis.

According to Lereboullet and Mouzon, tardy infantilism in the adult of pituitary origin, which was first described by Gandy in 1906, is characterized by the loss of the sexual characters of adult life, viz. loss of sexual function and morphological retrogression of the primary and secondary sexual attributes. The syndrome occurs during the height of genital activity between 20 and 40, and particularly between 30 and 35. The accessory symptoms which are usually present, according to Gandy, are: (1) some characteristics of myxoedema, such as swelling of the face, dry and ichthyotic skin, and partial or total loss of hair; (2) headache, sweating, polydipsia, and polyuria, which often mask the onset of the symptoms; (3) gynaecomastia; (4) smallness of the thyroid on palpation; (5) a previous history of syphilis. The syndrome is generally produced by a pituitary lesion, which may be due to adjacent bony lesions.

Lisser, of San Francisco, records five cases of pre-adolescent hypopituitary infantilism—two of the Fröhlich and three of the Lévi-Lorain type—in boys aged 10, 10, 14, 15, and 19, their corresponding mental ages being 3, 3, 7, 9, and 8. These boys showed complete absence of the prostate as far as could be determined by rectal examination, and two had a very diminutive prostate. Lisser suggests that the normal development of the prostate is in part at least dependent on normal pituitary secretion.

E. D. Friedman reports a case in a man aged 19 resembling that recently related by Reichmann (vide *Medical Science*, 1920, **2**, 135) in that deficiency of the anterior lobe of the hypophysis shown by stunted growth was associated with overactivity of the suprarenals, which was indicated by hypertrichosis, a high cholesterin content of the blood, and insufficiency of the thyroid.

A case of pituitary adiposity in a boy aged 13, which developed a few weeks after lethargic encephalitis is reported by Fendel, who states that no previous example of this complication of lethargic encephalitis has been recorded.

According to Tucker, professor of nervous and mental diseases, of the Medical College of Virginia, who has published three previous papers on pituitary epilepsy, convulsions in no way distinguishable from idiopathic epilepsy are caused by under-secretion of the pituitary gland. For the diagnosis of pituitary epilepsy three conditions are required: (1) the convulsions must appear during adolescence; (2) the case must present clinical evidence of hypopituitarism; (3) radiographic evidence of pituitary under-secretion must be present. A cure or considerable improvement is effected in these cases by administration of the whole gland extract in doses of from 6–12 grains daily.

Petényi and Jankovich record a fatal case of incipient acromegaly in a boy aged 10½, who presented the characteristic facial appearance and thickening of the phalanges, though all the other typical symptoms of acromegaly, including psychical changes, were absent. Death was due to tuberculous meningitis. The autopsy showed enlargement of the hypophysis, hyperaemia of the anterior lobe, much increase in the eosinophil cells, and colloid change in the middle lobe. All the other endocrine glands presented a normal appearance, both on naked-eye and on microscopical examination.

Zondek, who maintains that the relations between the circulatory system and the endocrine glands is much closer than has hitherto been supposed, has frequently found cardiac hypertrophy, especially of the left ventricle in acromegaly, accompanied by slight rise of blood-pressure and disturbance of the cardiac function. He attributes this to the tendency to increased growth originating in the hypophysis involving the heart, whereas in giantism, in which the tendency to increased growth finds free play in the extremities, the heart is not affected.

Pineal gland. Zandrén records the case of a boy aged 16½ years, who presented a number of abnormalities in development, viz. considerable retardation of physical growth, unerupted teeth, small testes, and absence of all secondary sexual traits. In addition to infantilism there was severe anaemia of a secondary type. Death took place from pneumonia, and the autopsy revealed complete absence of the pineal body, a normal condition of the thyroid, hypophysis, and suprarenals, and hypoplasia of the testes. The case was thus the exact opposite of macrogenitosomia praecox, which is associated with tumours of the pineal body.

Pluriglandular syndromes. Sehrt, of Freiburg, maintains that, owing to under-nourishment due to the blockade, important changes have taken place in the thyroid and suprarenals of the German population. He claims that thyroid insufficiency is manifested by an acceleration of clotting, relative and absolute leucopenia, and a relative lymphocytosis to which Lampe and Saupe have recently drawn attention (vide *Medical Science*, 1920, **2**, 137–8). Suprarenal involvement is shown by the low blood-pressure of otherwise normal persons. Lampe and Saupe recently examined a large number of healthy men and found the relatively low readings of 100–115 mm. Hg with Riva-Rocci's instrument. During the war Rostocki not infrequently found a blood-pressure of 90–100 mm. Hg in healthy resting soldiers. A tendency to post-operative haematoma which has apparently been very frequent in Germany during the last two years is also attributed by Sehrt to changes in the suprarenals. Finally, in many places during the last year the production of adrenalin had to be discontinued because none could be obtained from the suprarenals of the animals which usually supplied it.

At a recent meeting of the Société de Thérapeutique, Marie and Fourcade (1) read a paper on opotherapy and the menopause, in which they stated that suppression of the monthly periods was not the only cause of such mental disorders as obsessions, phobias, melancholia, acute hallucinations, and more or less systematized persecutional insanity which occurred at this time. They were inclined to assign the chief rôle to endocrine insufficiency, especially of the thyro-ovarian secretion. They therefore made a systematic use of opotherapy in all the mental disorders of the menopause. After a preliminary period of 10–15 days devoted to a general disintoxication, when a slight degree of hepato-renal intoxication was present, a combination of thyroid and ovarian extract was employed, supplemented by suprarenal extract or extract of other endocrine organs whenever signs were present indicating their insufficiency. The histories of eight cases are recorded, in six of which considerable improvement took place under this treatment and in two no result was obtained. At a subsequent meeting of the same society Marie and Fourcade (2) reported 10 cases with minor signs of Graves's disease who were benefited by pluriglandular opotherapy consisting in administration of extracts from the ovaries, corpus luteum and hypophysis.

Caussimon, of Bordeaux, reports a case of acromegaly in a woman aged 36, associated with signs of pluriglandular insufficiency, viz. symptoms attributable to the thymus, thyroid, and ovary. There was no enlargement or deformity of the sella turcica on X-ray examination. Out of 33 cases of acromegaly collected by Caussimon from the literature between 1886 and 1919, in 26 no mention is made of persistence of the thymus, in 4 the presence of characteristic retrosternal dullness is noted, in 2 a persistent thymus was found, and in 1 no trace of it was present *post mortem*. The thyroid in these cases was sometimes atrophied and sometimes enlarged. Occasionally there was exophthalmos. In the present case there was definite atrophy of the thyroid, and the development of the subcutaneous tissue, appearance and texture of the skin, and scantiness of hair resembled myxoedema. Disturbance of the ovarian function was shown by amenorrhoea which had been present from the onset, as in 30 of the 33 collected cases. The present case did not show any symptoms attributable to the suprarenals, and in only two of the 33 cases was involvement of these glands noted. Thus Motais states that his patient's skin became bronzed as in Addison's disease, and in Gilbert Ballet and Laignel-Lavastine's case the suprarenals were found to be full of adenomas *post mortem*.

Bertolotti records the case of a man, aged 35, who was admitted to hospital with all the signs of a rapid and malignant attack of acromegaly, viz. almost complete blindness, profound adynamia, sexual impotence, and advanced cachexia. X-rays showed a pituitary tumour the size of a small nut compressing the chiasma. The patient was subjected to radium treatment amounting in all to 7,360 mgm., distributed over eight séances in the course of four months. There was at first an aggravation of all the symptoms, but after about a month slow but progressive improvement set in, and finally a permanent clinical cure was established.

According to Leschke, growing old, at least in the human subject, is caused not only by extinction of the function of the interstitial generative glands, but in a still greater degree by suppression of the function of the other glands of internal secretion, among which the anterior lobe of the hypophysis and the suprarenal cortex play the most important part. In attempting to produce an artificial rejuvenation in man Leschke endeavours to stimulate the suprarenals, thyroid, and hypophysis by X-rays, and does not confine himself to stimulating the generative glands by ligature of the vas deferens, irradiation of the testes or ovaries, or transplantation of portions of these organs. In the estimation of the results of supposed rejuvenation Leschke recommends the exercise of considerable reserve, especially as one has to depend on the statements of patients who may have been influenced by the propaganda in the daily press.

Lereboullet reports three cases showing the benefit obtained in cases of sclerodermia by the association of thyroid, pituitary, and suprarenal extracts.

Bussi records a case of multiple sclerosis of the endocrine glands in a man aged 50 characterized by precocious senility, loss of hair, low blood-pressure, small thyroid, atrophy of the sexual organs, and pigmentation of the skin. The onset of the condition was accompanied by an attack of tetany indicating involvement of the parathyroids.

According to Naamé, of Tunis, the vomiting of pregnancy is due to autotoxaemia caused by thyro-ovarian insufficiency, and the cessation of vomiting towards the middle of pregnancy is the result of establishment of glandular equilibrium owing to hypertrophy of the thyroid. A rapid cessation of vomiting can be effected by thyro-ovarian opotherapy, which favours the development of this hypertrophy. The treatment consists in administration of tablets containing thyroidin 0·05 gm., ovarian extract 0·10 gm., three times a day for a few days.

Hämmerli, of the Geneva Pathological Institute, records a case of well-marked bilateral hyperplasia of the salivary glands with the first anatomical and histological description of the condition hitherto given, accompanied by a gigantic goitre weighing 1,050 gm. and hyperplasia of the suprarenals in a man aged 50, the subject of dementia praecox. He regards as probable the supposition that the salivary glands are closely connected with the endocrine glands, but thinks that further experimental work is required to prove this, and comes to the conclusion that, owing to our ignorance of the physiology of the salivary glands, an explanation of their hypertrophy in association with certain disturbances of function of the endocrine glands cannot be given at present.

Brock and Kay report three cases of pluriglandular disturbance in men aged 27, 20, and 23 respectively, associated with unusual manifestations in the muscular system, viz. muscular dystrophy in the first case, increased muscular strength out of proportion to the patient's height and stature in the second case, and myotonia congenita in the third case.

According to O. L. Levin, who records an illustrative case with a review of the literature, von Recklinghausen's disease is a complex of cutaneous and general symptoms depending entirely on endocrine dysfunction. The great majority of cases present definite signs of endocrine disorders and eventually die from progressive asthenia unless an intercurrent disease occurs.

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J. D. R.
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SOME RECENT OBSERVATIONS ON THE NERVOUS LESION IN EXPERIMENTALLY PRODUCED AVIAN POLYNEURITIS (EXPERIMENTAL BERI-BERI).

In an earlier number of this journal (1920, **2**, 241) an attempt was made to determine how far it was then possible to correlate the results of clinico-pathological and experimental studies on beri-beri. It was pointed out that as yet no satisfactory correlation was possible; partly because biochemical investigation was incomplete, and in part, also, because certain experimentally based inferences as to the pathogenesis of the disease did not harmonize with all the clinical and pathological facts of observation and failed to account for some of them. In the meantime, experimental research has been actively carried on, and therefore a fresh survey of some recent work may be of interest.

The points brought out in the earlier review may be summarized as follows: (i) The nervous symptomatology and lesions of beri-beri are not specific for this disease, but are indistinguishable from those of toxic polyneuritis, caused, for example, by alcohol or by the toxin of diphtheria. To these and certain other poisons the whole nervous system reacts by a widespread parenchymatous degeneration involving both nerve-cells and fibres. There are not, in the ordinary acceptance of the term, any inflammatory phenomena in the nervous system under these conditions, and hence their absence from the nervous system in beri-beri does not indicate that this is a new or unique form of nervous disease. Such a conclusion is erroneous and could have arisen only from an exclusive pre-occupation with this disease and from a neglect of the lessons of neuropathology. As the earliest investigators recognized, beri-beri, in respect of its nervous involvement, belongs to the category of the toxic polyneuritides. (ii) The symptoms of beri-beri are threefold: nervous, cardiac, and vasomotor. By the last-named is intended the oedema which often forms so striking a feature of the human disease, and for which no satisfactory explanation is yet available. In the acute pernicious form of the malady in adults (Hamilton Wright), and in some infantile cases, death is due to acute heart failure, and there are neither nervous symptoms during life, nor nervous lesions discoverable after death. Here the disease is purely cardiac, and the lesion myocardial. Probably some degree of cardiac involvement is constant in man, and it has been the custom to attribute the fatal cases of heart failure to vagus paralysis, notwithstanding that this is an inadequate and unproven cause. On the other hand, in diphtheria, which shares with beri-beri a remarkable liability to sudden heart failure, the essential lesion is almost certainly myocardial. There is no reason to seek for any other explanation for the phenomenon when it occurs in beri-beri. (iii) Any satisfactory hypothesis of the causation of beri-beri must necessarily include both nervous and myocardial lesions. Clearly no hypothesis of nervous system degeneration from vitamin deprivation meets the facts of the case in the human disease, however completely it may appear to do so in the case of avian polyneuritis. (iv) In view of its striking resemblance, clinically and pathologically, to the toxic polyneuritides, with their associated myocardial involvement, the neurologist naturally seeks for some more adequate and positive cause for this reaction of the tissues than the mere absence of an accessory food factor from the diet. A second factor is essential, and there is increasing evidence, recently added to by Findlay (2), that a disorder of carbohydrate metabolism is an essential part of beri-beri. A possible and satisfactory explanation of the disease in all its varied forms would be the action of a poison produced in the body in the course of this disordered metabolism. Such a possibility has been neither explored nor excluded, and if adopted as a hypothesis has the unique merit of not being incompatible with any of the facts of observation, experimental or clinical.

However fundamentally important these considerations are for the clinician and pathologist, it is perhaps inevitable that they should fail to impress the biochemist, pre-occupied as he necessarily is with a single and somewhat abstract aspect of the problem. That they have not weighed with him is apparent from the light-hearted fashion in which certain of them were disposed of by the opener of the discussion on the rôle of vitamins in medicine at the annual meeting of the British Medical Association at Cambridge in 1920 (*British Medical Journal*, 1920, ii, 147), and from the alternative explanation which he offered.

Findlay's hypothesis, which we are about to discuss, appears to show a similar disregard for the lessons of clinical and pathological observation. This fundamental difference of outlook depends upon the question of the essential nervous lesion in beri-beri and upon the relation of this lesion to the clinical manifestations. It is quite certain that these debatable points can never be resolved by the exclusive study of beri-beri, much less of its avian form, nor upon the basis of a knowledge of neuropathology limited to this disease.

The essential lesion in the nervous system. In this connexion it is polyneuritis so-called which we have to consider, and not simply beri-beri. It has long been known that chromatolysis and other changes in the cell-body occur in the nerve-cells in the condition so named. Oppenheim, Strümpell, and other authorities have taught that multiple neuritis is a general disease of the nervous system with a selective action upon certain groups of neurones. The presence of such cell lesions in avian polyneuritis has even been adduced by Lhermitte as an additional indication that the condition belongs to the category of toxic polyneuritis. The teaching in this respect is well reflected in the observation of Cole (1902): 'In alcoholic neuritis, as in other forms of toxic neuritis, the degeneration of peripheral nerve-fibres does not stand alone, but is associated with a more or less characteristic type of change in the related cell . . . this combination of fibre degeneration with cell change is, at least in many acute cases of the disease, not confined to neurones which go to make up peripheral nerves, but is exhibited by neurones of various groups situated entirely within the brain and cord. The disease is something more than a mere peripheral neuritis, and represents a widespread affection of the whole nervous system.' We need not labour the point, and it is clear that the stress laid in recent experimental work on the nerve-cell changes is without special significance, and brings the disease into line with toxic polyneuritis, rather than establishes it as something mysteriously different. Intimately bound up with this question of the essential lesion is the further one of **the relation of the nervous lesions to the symptoms.**

Here we have one of the most difficult problems in neuropathology, and again, one which cannot be settled by the exclusive study of paralysed birds. The interpretation of their symptoms is not easy, as the conflict of opinion on the subject clearly indicates. We must also study paralyses in man to gain an insight into the matter. A single example will suffice to show how difficult it must always be to correlate precisely and in a quantitative sense the clinical symptoms with histologically discoverable lesions. From the study of the spinal cords in several fatal cases of compression paraplegia, Gordon Holmes found that the degree of descending pyramidal tract degeneration, contrary to expectation, was minimal. It is a common experience at autopsy to find lesions for which there were no corresponding disorders of function during life. This applies particularly to chronic and long-standing maladies. On the other hand, in rapidly developing diseases, impairment of function may ensue before the microscope reveals any lesion. Therefore the attempt to correlate precisely the proportion of degenerated nerve-fibres in the sciatic nerve of a pigeon with the degree of paralysis observed before death is foredoomed to failure. The fact, recorded by Vedder, McCarrison, and Findlay, that healthy birds may show numerous degenerated fibres in their nerve-trunks makes this obvious. In old cases of human beri-beric paralysis some such relation may well obtain, but in the day-old paralysis of a pigeon, who would expect to find extensive associated nerve degeneration? The almost immediate cure of such a paralysis on appropriate feeding indicates clearly that no gross lesion can have been responsible, and it must not be overlooked that nerve degeneration is a gross and even a terminal phenomenon. Function must be impaired before histological changes are apparent, and it is to the recovery of fibres not structurally destroyed that we must attribute the rapid restoration of power in birds under these conditions. Therefore, we cannot assume that histologically normal fibres are necessarily capable of conduction, or that the proportion of degenerated fibres found in any particular case represents the sum total of fibres out of action. Consequently, there is no particular mystery in the development of paralysis before degeneration is obvious, or in the persistence of degenerated fibres after cure of paralysis.

Nevertheless, the observers we have named all conclude, from their inability to correlate nerve-fibre degeneration with paralysis, that the essential lesion and the true cause of paralysis must be the abnormal appearances in the nerve-cells in avian polyneuritis. Not only is the conclusion unnecessary, but it has little foundation. Chromatolysis is much more rapidly and easily produced than nerve-fibre degeneration. Pyrexia, infection, exhaustion, and other factors all lead to abnormal appearance in the cell-body, but these have no clinical counterpart. Oppenheim, writing in this connexion, has emphasized that such changes are not necessarily degenerative, or productive of paralyses. In human diseases in which true degeneration of nerve-cells in brain and cord is the essential lesion, the symptomatology is quite other than that of polyneuritis or beri-beri. If a functional inactivity of nerve-cells in the brain is the essential beri-beri nervous lesion, why do we never see cranial nerve palsies, hemiplegia, hemianaesthesia, visual defects, speech disturbances, or mental disorders, or indeed a single unequivocal cerebral or brain-stem symptom? It is astonishing that those who hold chromatolysis responsible for all the symptoms have never asked themselves this question. Further, judging from analogy, there can be no reasonable doubt that the nervous symptomatology of beri-beri corresponds to that of peripheral nerve lesions. Therefore we may conclude that it is entirely erroneous to regard the abnormal appearances in the nerve-cells as the only essential lesion and the exclusive cause of the nervous symptoms in beri-beri. The fallacy is one we must expect when we demand from histology more than it is capable of telling us. We believe that a wider experience of the difficulties of nervous system histology and of the pitfalls which beset its interpretation would have prevented the adoption of these fallacious conclusions. In the introductory chapter of Buzzard and Greenfield's recently published text-book of neuropathology, the experimental worker engaged in this fascinating problem of nutritional disease, and thus brought face to face for the first time with the reaction of the nervous system to morbid agents, will find a more correct orientation than he appears so far to have achieved.

We are now in a position to consider the special features of Findlay's hypothesis of the pathogenesis of beri-beri. He believes that the nerve-cell changes we have referred to are the essential lesion of beri-beri and the true cause of the paralysis. He assumes that chromatolysis is a sign of nuclear inefficiency and starvation, and that the paralysis therefore depends upon nuclear starvation. He quotes McCarrison's observations to the effect that the adrenals are enlarged in avian polyneuritis and that the enlargement is mainly cortical. Findlay believes that the enlargement depends upon an increased storage of phosphorized lipoids, which are essential for the synthesis of nucleic acid. The adrenal cortex is normally a storehouse for these substances, which, however, the nucleus can only utilize in the presence of vitamin B. When the tissue content of vitamin falls below normal, the lipoids are immobilized in the adrenals instead of being passed on to the nervous system. The nervous system then begins to run short of nuclear material and a functional paralysis results. If the shortage becomes acute the vital centres in the medulla are at length paralysed and death ensues.

Brief consideration reveals the illusory nature of these assumptions. We cannot say that chromatolysis indicates nuclear starvation, or that it can give rise to paralysis. The view that enlargement of the adrenal cortex in avian polyneuritis results from the storage in its substance of phosphorized lipoid rests, as Kellaway has shown, upon scanty and inconclusive evidence. There does appear to be a slight increase of cholesterol in these circumstances, but for the other phosphorized lipoids the matter has never been investigated. The similar morphological changes in the adrenals which have been described in starvation indicate that, whether the adrenal cortex acts as a store-house for phosphorized lipoids or not, such a storage cannot be correlated with nervous system degeneration and beri-beric symptoms. As for Findlay's comparison of Addison's disease with beri-beri, we fail to find a single point in which the analogy is apt. Finally, the assumption that death in beri-beri results from paralysis of vital medullary centres is contrary to every indication and has no basis whatever, while there is no place in his theory for the cardiac involvement we have referred to.

In short, it seems that the exclusive study of an experimentally produced avian modification of a human disease has led to certain misconceptions which might have been avoided by a broader outlook on the problem. Human beri-beri is a much more polymorphic disease than its experimental counterpart, and in this respect is not peculiar among human diseases. Clinical problems are always more complex than pre-arranged and clean-cut experimental ones. Nevertheless, the clinical manifestations of disease in man are much more easily assessed than their imperfect reproduction in an animal far removed from him in the scale of life. The paralytic symptoms of polished-rice fed pigeons appear particularly difficult of interpretation. Take, for example, the so-called cerebellar symptoms of avian polyneuritis. Are they really cerebellar? Might they not equally well be vestibular and peripheral? Kimura believes that they are a manifestation of general starvation and can be abolished by forcible feeding, while Shimazono says that they occur as agonal symptoms in birds dying from other causes and have no localizing value. Similar differences of interpretation obtain for the head retraction so often seen, and whatever be the truth there is no doubt that the interpretation is uncertain, and that by the exclusive study of birds we have lost the valuable analogies which the observation of human paralyses affords.

If these views be correct, we may conclude that we are still far from any correlation of opinion among investigators of the different aspects of the problem. We venture to think this is inevitable until the biochemist lays under contribution the sources of information to be derived from clinical and pathological observation. Beri-beri, in which both physician and biochemist are deeply interested, bears many striking resemblances to a form of disease known to result from the action of certain poisons, and not, so far, known to result from any other cause. There are numerous indications as to where we might, with hope of profit, look for the formation of a similarly acting poison in beri-beri. It would be singularly unfortunate if a rigid adherence to the conception of simple vitamin starvation as a satisfactory explanation of the whole disease prevented the exploration of this possibility.

There is a useful moral to be drawn from *the history of research on beri-beri.* The earliest observers, impressed by the symptomatology and morbid anatomy of the disease, concluded that it must be due to infection by a micro-organism, or to intoxication from the consumption of noxious food. No other conclusions were open to them at that time, but repeated researches failed to substantiate the existence of either factor. A period of speculation followed and produced nothing more satisfying than the suggestion that inhalation of some mysterious air-borne virus was responsible. Then came Braddon's incrimination of rice as an important factor (1906), followed by Fraser and Stanton's discovery of the true nature of this association (1909), which established upon a sound basis the conception of selective food-deprivation as a cause of disease in man. Subsequent experimental workers have laid bare many of the nutritional laws concerned in this as in other deficiency diseases, and in solving the problem of beri-beri prevention have laid practical medicine under a deep debt of gratitude. But in discarding the unsound infective and intoxication theories of the pioneer workers, modern experimental observers have also rejected the very sound pathology of their predecessors, apparently assuming that because the early conceptions were not entirely correct they were completely wrong. Hence in the course of some forty years they have abandoned a sound pathology and some erroneous theories of causation in favour of a scientific aetiology and a most unsound, theoretical, and avian pathology, primarily designed to meet the needs of an immature theory. This, indeed, is the halting mode of progress typical of many other branches of science, and our present task is to reconcile the new theory of causation with the old pathological and clinical conception of the disease. There should be no insuperable difficulty in doing so, as soon as we realize that the theory, rather than the facts of observation, is the uncertain factor, and that beri-beri is no simple matter of nervous system degeneration from starvation, whether of vitamin B or of phosphorized lipoids. Once we conceive it possible that a second factor is present, and this of toxic nature, a satisfactory correlation of observations seems within reach. It has been suggested that this insistence upon a second and positive factor is nothing but the expression of an inherent inability, on the part of those who think in terms of pathology, to imagine a purely negative causation of disease. But it is evident from the considerations brought forward in this review that we need not delve in the subconscious mind of the pathologist for the basis of his objection to the single factor interpretation of the vitamin theory. The scope and limitations of negative factors in the production of disorders of function in the nervous system have been a part of neurological tradition since Hughlings Jackson formulated the conception over forty years ago. It is because the conception is inadequate to account for all the observed phenomena in beri-beri that we reject it as a satisfactory explanation.

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F. M. R. W.

ABSTRACTS

SURGERY

Sloan, H. G. Successful end-to-end suture of the common carotid artery in man. *Surg. Gynec. & Obst.*, 1921, **33**, 62–5.

Harry G. Sloan, of Cleveland, reports successful suture of this vessel in a man aged 56 in whom the wall of the artery had been damaged during an operation for recurrent epithelioma. In attempting to stop the haemorrhage the sclerosed arterial walls were badly injured by haemostatic forceps over an area $\frac{3}{4}$ cm. long and extending over about half the circumference.

In view of the danger to cerebral circulation due to ligation of the common carotid at this age, it was determined to attempt to repair the vessel. The artery was exposed, clamped above and below with rubber-covered carotid clamps, and the injured area, 8 mm. long, was excised. The loose adventitious tissue was cleaned off the cut ends, and the latter joined by three guy sutures through all the coats, followed by a continuous over-and-over suture joining the cut ends of the vessel. Straight No. 16 needles, held on mosquito haemostats, and triple 000 linen split 12 times, were used; both were well lubricated with vaseline. The suture line was reinforced by stitching deep fascia over it. Although the patient's vessels were sclerosed, his blood-pressure 156 mm. Hg systolic and 100 mm. Hg diastolic, and although during the operation the right common carotid was blocked for 30 minutes, the patient made an uninterrupted convalescence.

The writer quotes other successful cases, viz.:

(1) V. Parczewski (*München. med. Wchnschr.*, 1916, **63**, 1646)—man of 21 years with arteriovenous aneurysm—$2\frac{1}{2}$ cm. of common carotid artery removed and the cut ends joined by circular suture. No neurological symptoms followed.

(2) H. von Haberer (*Wien. klin. Wchnschr.*, 1918, **31**, 285) reports one lateral suture of common carotid for aneurysm and four circular sutures for aneurysm following war wounds.

(3) Lexer (*München. med. Wchnschr.*, 1918, **55**, 468)—3 cm. resected—common carotid blocked for one hour during the operation. Paralysis of opposite leg cleared up the same evening, but paralysis of arm on same side took four weeks to disappear.

(4) Denk (*Wien. klin. Wchnschr.*, 1918, **31**, 285)—removal of 2 cm. of common carotid followed by circular suture in a man aged 20. In this case, and in Sloan's own case the early return of the temporal pulse, indicating patency of the carotid, is noted; in the other recorded cases this is not mentioned, and a certain amount of doubt therefore exists about the restoration of circulation in the circularly sutured carotid artery. C. C. C.

Royal Society of Medicine. Discussion on the medical and surgical treatment of Graves's disease. *Proc. Roy. Soc. Med.*, 1921, **14** (Clin. Sect.), 1.

Dr. H. Mackenzie, in opening the discussion, stated that no one would question the value of medical treatment, but all would admit that as yet nothing had been found which could claim to be a specific for the disease. His views as to the value of surgical treatment had changed considerably from those he had held ten years ago. His experience of the value of surgical treatment dated from 1915, when Mr. Dunhill first undertook the treatment of one of his cases. Since that time he had acquired a comparatively wide knowledge of the results of surgical treatment, and during this time no attempt had been made to select slight or early cases. The leading principles of selection had been (*a*) that the disease had lasted some time; (*b*) that a fair trial had been given to medical treatment; (*c*) that no real improvement had been brought about. The mortality for private and hospital cases had been under 2 per cent., and this in spite of the fact that often the operation had been performed almost as a forlorn hope. The results had been very satisfactory, and it was usually noticed: (1) that the patient became tranquil and ceased to be restless; (2) that there was a gain in strength and endurance; (3) that the heart's action became slower and steadier. Exophthalmos was the most persistent symptom, but the staring frightened look usually disappeared. In cases in which only one lobe had been removed the improvement was usually not so great as in those in which a smaller amount of the gland had been left behind, and a second or even a third operation might be needed.

As possible contra-indications he gave: (1) where there was much fear or dread of the operation; (2) when mental symptoms were present; (3) when Graves's disease was associated with diabetes; (4) when there was auricular fibrillation.

He advocated strongly the use of local anaesthesia. In his experience X-ray treatment had not been of much value. He quoted one case where all the signs of Graves's disease were lost and the patient instead presented early signs of myxoedema, but he had not had another case which he could consider cured, and on the whole regarded the results as disappointing.

Mr. J. Berry described his experience at length, and stated that wider knowledge had led him to be somewhat less sanguine than he had been in 1914. He stated that within a very short space of time after operation the patient felt that she had derived immense benefit. Many of the symptoms diminished or disappeared, but, although the exophthalmos was often lessened, complete disappearance was less common. The amount of benefit depended largely upon the amount of gland that had been removed.

The operation, except when skilfully performed, involved considerable danger to life which was far greater than of operations for simple goitre. It generally involved a mortality of from 3 to 5 per cent. In discussing the operative measures he stated that in his opinion partial thyroidectomy and ligation of the thyroid arteries were alone of any value. He had treated 28 cases by ligature of the artery, and now always ligatured the superior thyroid artery as it was much the simpler, and in fact a very safe operation. Considerable improvement had followed, but it was usually necessary later to perform a partial thyroidectomy. Here, he had almost abandoned the practice of operating simultaneously upon both lobes.

In discussing the question as to when operation should be performed he stated that he considered it wrong to perform thyroidectomy when there was acute mental excitement, or when myocardial degeneration was very marked, although in some cases a preliminary ligation was permissible. An operation should never be performed until the patient had been resting in a hospital or nursing home for some days. He did not operate if the patients were improving or if they did not feel at all ill. As regards the question of anaesthesia he was coming more and more to believe that light open ether was the most suitable, and he did not regard a local anaesthesia as the only factor of safety, or even the main one. He believed the chief cause of death was haemorrhage.

In the after-treatment the most important factor was the administration of large quantities of water. In summarizing his results he found that of 79 operations 53 were practically well; 18 were much improved; 3 were but little, or not at all, improved; 1 was worse, and 3 died.

Mr. T. P. Dunhill discussed three aspects: (1) The grounds upon which he considered some intervention other than purely medical to be necessary. (2) What degree of improvement could be obtained by surgical methods. (3) What permanence one might expect in this improvement. He discredited Sir William Hale-White's figures because 15 patients who had been admitted to hospital and died were excluded from the statistics. He laid stress upon the fact that death was not the only danger in Graves's disease. Serious disabilities might arise in advanced cases, but surgery was not to be undertaken until every toxic focus had been removed, until the patient had had a long rest, and until symptomatic drug treatment had been given a sufficient trial.

His personal experience of X-ray treatment had been unsatisfactory, for the pulse-rate had not come down, the size of the gland had not been reduced, the exophthalmos had not been altered, nor had the tremors disappeared. He quoted some cases where an operation had been performed when the patient was profoundly ill, and yet good results had followed operative treatment. In discussing the degrees of improvement that might be obtained, he also quoted a number of cases who were able to go back to a normal life and to carry out heavy duties and undertake a considerable amount of strain without ill effects. He laid stress upon the fact that a cure could not be expected after removal of only one lobe, but at the same time there was considerable danger in attempting to remove sufficient of the gland at one operation. In some cases it might be necessary to perform three operations.

Sir William Hale-White published statistics attempting to show that the life-history of those afflicted with exophthalmic goitre was no worse than that of normal patients. After deducting cases that could not be traced there remained 102 for consideration. Contrasting the after-history of these with that of healthy females of the same period of life, it appeared that their mortality was twice as great as it should be, but he believed that even this was too high.

Dr. S. J. Goodall laid stress upon the importance of the condition of the heart and of the use of Benedict's machine in testing the basal metabolic rates. He had come to the conclusion that the common cause of death in Graves's disease was ventricular fibrillation. The dangerous case was that in which there was definite myocardial degeneration, and in which the blood-pressure was high.

Mr. D. Armour said that his experience of the surgical treatment extended over fifteen years and included some 200 cases. He had found that rectal ether was a very suitable anaesthetic, and in many cases he had followed Crile's method of 'stealing the gland', the ether being administered per rectum. He laid stress upon the fact that chloroform should never be used. In performing the operation the greatest care should be used to avoid injury to the recurrent laryngeal nerve. He had always acted empirically and removed one lobe, the larger if they differed in size, together with the isthmus. He believed that the ligature of arteries had a definite place either as a preliminary to future gland removal, or as the only operation necessary. He contented himself with ligature of the superior vessels, either at one or two sittings.

Dr. F. Stoney had collected 200 cases which had been treated with X-rays. They consisted either of primary Graves's disease or of Graves's disease following old bronchocele. An investigation of the list of cases revealed the fact, however, that only very few of them had any exophthalmos, and it is very doubtful whether they would usually be included as true cases of Graves's disease. The disease she stated had in all of the men, 15 in number, been due to war conditions. She believed that X-rays would surely bring about partial atrophy of the thyroid, and that the atrophy could be pushed to any extent that might be desired. In recent cases a cure might be brought about with very few exposures, but in long-standing cases the treatment had to be much prolonged, and it was here that it was possible that surgery might be the best as it was more rapid.

Dr. J. M. H. Campbell reviewed a series of 127 cases, 89 of which had been traced. Of the 127, 8 had died in hospital of Graves's disease and one with carcinoma of the pancreas. Of the 80 who had been traced 7 had died of exophthalmic goitre since leaving hospital, 7 cases had been completely cured, 26 had been almost cured, 29 had been much improved, and 11 little, if at all, improved. He contrasted a series of 16 cases who had been operated upon with 56 cases that had only had medical treatment. These were grouped as follows:

	After Partial Thyroidectomy.	After Medical Treatment.
	Per cent.	Per cent.
Cured or almost cured	38	41
Much improved	38	28
Not improved	12	17
Died	12	14

He admitted, however, it was impossible to base definite conclusions on so few results.

Mr. W. H. C. Romanis laid stress upon the fact that with mild cases medical treatment should always be administered first, but in more severe cases it should only be used as a preparation for surgical treatment. He did not consider cardio-vascular symptoms in any way contra-indicated operation, but if mental symptoms were present operation did not hold out a reasonable prospect of improvement. Operation should not be urged when the patient was very unwilling to undergo it.

In discussing the operative procedures, he considered that removal of large portions of the gland was the method of choice. It was not sufficient to remove half the gland: one lobe, the isthmus, and at least a quarter of the other lobe was the minimum amount that should be excised. In severe cases it would not be desirable or possible to remove as much as one would wish at first, and a second or third operation might have to be done later.

The mortality was somewhere about 2·5 per cent. As a rule there was more improvement in the subjective symptoms than in the physical signs, and this often occurred within a day or two after operation. After several weeks an improvement in the physical signs commenced. He had never seen any symptoms which appeared to be due to the interference of the parathyroids.

Mr. A. J. Walton first of all brought forward evidence that the disease was due to hypersecretion, and that results of medical treatment were unsatisfactory. He discredited the value of Sir William Hale-White's figures since only 102 cases had been traced out of 200, and even these did not include a series of 18 cases that had died in hospital. He did not advocate operation in the first six months of the disease as it was in this period that beneficial results might accrue from other measures. His own experience of X-rays had been that they were of but little, if any, value. He laid stress upon the danger of this form of treatment, and quoted cases where it had led to considerable disfigurement from the formation of widespread telangiectases. One case had developed carcinoma of the skin. He regarded medical treatment as a most important preliminary to operation.

In discussing the question of the time of operation, he laid stress upon the importance of selecting that period at which the symptoms were in relative abeyance. He had found that better results were obtainable in what he designated as the vascular type, which was generally seen in young women, and where the thyroid was large and there was a rapid pulse and well-marked exophthalmos. In the second or nervous type it occurred in more elderly patients with a smaller thyroid and fewer cardiac symptoms, and the results were not so satisfactory.

In discussing the choice of operation, he stated that in his experience partial thyroidectomy had been the method of choice. He had found that general anaesthesia with ether had been the most satisfactory, especially if the anaesthesia had been induced by the administration of the ether per rectum. He had found that after operation there were four periods: (1) a stage of reaction which lasted two or three days; (2) a stage of primary improvement which lasted two or three weeks; (3) a stage of relapse which might persist for two to nine months; (4) a stage of apparent cure and a stage of complete cure. He had found that 75 per cent. of the cases had been changed from disabled wrecks into people living normal lives and capable of earning their own living.

Dr. Hernaman-Johnson, in discussing the effects of X-rays, held that it was an unjustifiable procedure, now that the mortality of operation had been reduced, to attempt the reduction of thyroid secretion by producing cell destruction and fibrosis with X-rays; but he believed that very great constitutional benefit might be gained thereby, and that X-rays applied anywhere to the body induced a resistance which was not specific.

A. J. W.

Berry, James. On a further series of 500 goitre operations with special reference to after-results. *Proc. Roy. Soc. Med.*, 1921, **14** (Surg. Sect.), 89; also *Brit. J. Surg.*, 1920–21, **8**, 413.

Berry devoted this paper to a careful review and analysis of his cases, and included all cases in which he had removed any portion of the thyroid gland during the period from January 1, 1913, to December 31, 1919.

The cases were 500 in number and formed a direct continuation of a previous series. His analysis of the sex and age incidence showed only about 12·5 per cent. of the patients were males, and the age at which the disease was most common was between 30 and 50. Five girls, however, were only aged 14. These were all examples of parenchymatous goitres which were causing dyspnoea and failing to respond to medical treatment. Operations in children below the age of puberty were hardly ever necessary and should never be undertaken except for some specific reason. Among the male patients, 7 were over 70 years of age and all made good recoveries.

In considering the pathology of the lesion he found that 198 cases were encapsuled lesions, adenoma, or cysts, and 302 were non-encapsuled. These included 13 examples of malignant disease. He states that pathologically the above classification is not strictly accurate but is convenient clinically. He lays stress upon the inefficiency of modern classifications, but points out that the terms in use are of clinical value. The series only includes 3 cases of inflammation. There were, however, 79 operations for exophthalmic goitre, and he points out that these cases should be sharply distinguished from false exophthalmic goitres, that is, localized lesions which may give rise to tachycardia and tremor but never show any exophthalmos. Of the malignant cases some were of the papilliferous variety, one was an endothelioma, and two were sarcomata.

In this group the first sign for operative interference was dyspnoea, 74 operations being undertaken for this cause. Discomfort and deformity or hyperthyroidism were the next most frequent indications. In discussing the question of dyspnoea he points out that when long persistent it may lead to other complications, such as dilatation of the heart, tachycardia, and chronic lung trouble. In no case had he to perform a tracheotomy, as he holds very strongly that the removal of the source of the pressure, namely, the goitre, is a far more satisfactory procedure. He points out, however, that after the goitre has been removed there is sometimes a danger of tracheal collapse. When the trachea is bilaterally compressed the removal of one lobe may be quite insufficient to relieve the dyspnoea or indeed may make it worse, as this may lead to kinking, which usually causes fatal suffocation. He also points out that a unilateral enlargement of the thyroid may be considered the cause of the dyspnoea, whereas the opposite lobe, which may be the real offender, may lie deep behind the sternum within the thorax. He lays stress upon the difficulties of diagnosis in doubtful malignancies and states that a positive diagnosis of malignancy is almost impossible, although there may be points which give rise to suspicion. It is important, in making a diagnosis, to determine whether the thyroid moves upon the larynx or the trachea, for in the malignant cases it is likely to be fixed. He gives a full review of the operations which have been undertaken for the different varieties of disease and also a full description of his method of removing an intrathoracic goitre. In nearly all cases drainage was employed and in only 7 of the 500 cases was it omitted. The mortality was extremely low, for there were only 2 deaths in the simple goitres, 3 in the exophthalmic goitres, and 2 in the malignant diseases. Of the 500 cases he had traced all but 14 cases. Of the total 342 of the simple goitres, 53 of the exophthalmic goitres and 5 of the malignant cases were quite well. A. J. W.

Freeman, L. A. A 'tourniquet' operation in toxic and other goitres. *Ann. Surg.*, 1920, **72**, 161.

Bilateral resection of a portion of the thyroid gives much more satisfactory results, both as regards the cosmetic appearance and because diseased glandular tissue is less liable to be left behind. The drawback of this method is the large amount of haemorrhage which may take place. The author describes his method by which the bleeding may be controlled. A narrow pair of alligator forceps is passed through the base of the elevated lobe and a thin rubber band drawn through. Three loops of rubber are thus drawn through the base of the lobe, one at either end and one in the middle. A piece of stout wire is now threaded through the ends of the loops. One end of the central loop is drawn tight and clamped close to the wire so that the elasticity of the band pulls the two wires tightly against the base of the lobe. At the two ends of the lobe the bands are wrapped round the projecting ends of the wires instead of being clamped. By this means the whole base of the lobe is tightly gripped by the two wires and the projecting portion of the lobe can be excised and the cut surface sutured with a haemostatic suture. A. J. W.

Moore, R. F. Exophthalmos and limitation of the eye-movements of Graves's disease. *Lancet*, 1920, ii, 701.

There has always been doubt as to the cause of exophthalmos in Graves's disease. Moore describes the three common theories: (1) that it is due to irritation of the sympathetic nerve; (2) to engorgement of the orbit with blood; (3) to an increase of the orbital fat. He says it is still stated that the exophthalmos disappears after death, which would support the first two theories. In a case which he saw after death the exophthalmos was still present. He reports a case in which the exophthalmos was so marked that it was necessary to undertake some procedure to save the eyes. The lids of the right eye could not be sutured. He therefore made an incision through the inferior conjunctival fornix and was able to remove a large quantity of fat, after which the lids were easily approximated. He noticed that, in addition to the excess of fat, the fat itself was very oedematous, as were also the inferior, internal, and external recti muscles. He deduces from this that the usual cause of the exophthalmos is an increase of fat and the limitation of movement is due partly to the pushing forward of the eye and partly to the oedema of the muscles. A. J. W.

Kendall, E. C. Chemical influence of the active constituents of the ductless glands. *Surg. Gynec. & Obst.*, 1921, **32**, 205.

In 1914 Kendall was able to separate the iodine-containing compound of the thyroid in pure crystalline form. Since that time a good deal of work has been carried out by him concerning the exact chemical properties of this compound, which he has named thyroxin. He states that it is a white crystalline substance, very weakly acid, and is extremely insoluble in water but readily soluble in sodium hydroxide. It contains 65 per cent. of iodine, which is very firmly attached to the organic nucleus, from which, however, it is easily broken off by the action of sunlight. It is separated with difficulty by boiling the entire gland in 5 per cent. sodium hydroxide. When acid is added practically everything is held in solution except the thyroxin. By this means an impure precipitate is prepared, from which pure crystalline thyroxin is separated with difficulty. This is accomplished by taking advantage of its insolubility in alcohol and of the fact that the impurities form salts with barium.

He claims that thyroxin will bring about all the changes in a thyroid-deficient individual that are brought about by desiccated thyroid. He finds that it has no effect on the blood-pressure and that there is no marked physiological response immediately, but Plummer has shown that the maximum effect is reached about the tenth day in a myxoedematous patient. The effect of a single injection is continued for at least twenty-four days.

His investigations of the amount of iodine within the blood tissues seems to show that most of the iodine in the blood-stream is in the form of thyroxin and the iodine contents of the tissues is much higher in winter than in summer. The physiological dose is from $\frac{1}{50}$ to $\frac{1}{75}$ milligram per kilo of body-weight, but when one thousand times as much as this was given to a small dog there was but little effect. The excess appears to be excreted before it has time to function. It appears to be chiefly excreted in the bile. If administered in repeated small doses the animal will die with a maximum degree of hyperthyroidism. A. J. W.

Torraca, L. L'influenza dell' irradiazione solare in alta montagna sul processo di guerigione delle ferite. [**Influence of solar irradiation in high mountains on the healing of wounds.**] *Arch. ital. di Chir.*, 1921, **3**, 441–52.

Experiments on guinea-pigs lead to the conclusion that, apart from any bactericidal power, solar irradiation exercises a favourable biological action on aseptic wounds, cicatrization of which is definitely hastened.

E. R. C.

Macaggi, G. B. Sul livello di biforcazione del nervo tibiale posteriore. [**On the level of bifurcation of the posterior tibial nerve.**] *Arch. ital. di Chir.*, 1921, **3**, 507–16.

Normally the nerve divides 1·5 cm. above the tip of the malleolus, whilst the artery of the same nerve divides three cm. lower, or on the level of the sustentaculum, after it has crossed the internal plantar nerve. The arterial division is very constant in level, but the nerve in 13·5 per cent. of cases divides much higher than usual and by as much sometimes as 8·5 cm. To expose the nerve it is advisable to use, not the semilunar incision customary for the artery, but a vertical one above it. E. R. C.

Cunningham, J. H. Focal infections with metastatic manifestation, with special reference to gonorrhoeal arthritis. *Surg. Gynec. & Obst.*, 1921, **32**, 501.

The author reports good results in gonorrhoeal arthritis from removal of infected seminal vesicles and drainage of the prostate. The inability to demonstrate *Gonococcus* in the vesicles or in the prostatic secretion is, in the author's opinion, no contra-indication to the operation, as the *Gonococcus* may be masked by secondary staphylococcal infection. The seminal vesicles are approached and removed by the perineal route. The vas is drained by incising the ampulla. The prostate is drained by multiple deep incisions into its posterior surface.

Results have been published of 128 cases in the *Journal of Urology*, August 1919.

Sterility without impotence results. J. T.

Papin, E. La pyélographie. [**Pyelography.**] *Rapports du Premier Congrès de la Soc. Internat. d'Urologie*, Paris, 1921, 230.

Papin uses the following solution:

Sodium bromide	300 gm.
Distilled water	700 c.cm.
Oxycyanide of mercury	1 cgm.

The oxycyanide is added to make the solution antiseptic. Sodium bromide solution has the advantages that it is clear, it does not stain, it is not toxic, and it is relatively cheap; in the event of absorption into the renal parenchyma it is probably better that a soluble crystalloid, which can be easily washed away, should be used than a colloid, the particles of which will remain in the kidney.

A large ureteral catheter should not be used, so that the fluid can readily flow back beside the catheter into the bladder and excessive pressure thus be avoided. In most cases Papin uses a No. 12. An opaque catheter should always be used in order that the surgeon may be able to see that the end has not met with an obstruction. In general the ureteral catheter should be pushed into the renal pelvis; if it is arrested before reaching this, the injection can still be made or the fluid may run back into the bladder; this reflux can be determined if a vesical catheter has been passed. In rare cases it is not necessary to pass a ureteral catheter, simple vesical injection serving to fill both ureters and pelves.

The liquid should never be injected with a syringe, as in this case the pressure of injection is unknown; on the method of injecting depends the harmlessness or danger of pyelography. Papin runs in the fluid from a Mohr's burette and makes the radiographic examination. If pain is severe it can immediately be relieved by aspirating some of the fluid with a syringe; injection under general anaesthesia or under morphia is an extremely dangerous practice.

The pain produced by injecting the fluid varies in different cases; usually the smaller the pelvis the greater the pain. Its onset may be sudden or slow; it does not cease simultaneously with the discharge of liquid from the pelvis, and may even temporarily increase after the emptying of that cavity. It is situated below the false ribs in the axillary region and radiates back to the costo-lumbar angle and forward towards the iliac fossa. There is commonly a rise of temperature, usually slight, on the same evening, which disappears on the third day; this seems to be less frequent since sodium bromide has been substituted for collargol. F. J. F. B.

Berti, G. Ricerchi sperimentali e considerazioni cliniche sulla resezione parziale e sull' ipertrofia compensatoria del rene. [**Experimental researches and clinical considerations on partial resection of the kidney and compensatory hypertrophy.**] *Policlin.*, 1921, **28** (Sez. Chir.), 289.

The author's experiments were carried out on rabbits, and showed that whilst compensatory enlargement of the remaining kidney substance is observed and is roughly proportional to the loss, it is confined to the secreting portion of the tubules, which are elongated, the epithelial cells showing great karyokinetic activity; no new tubules or glomeruli are to be found. In man, whilst resection is satisfactory and of fairly wide application, it is wise to limit the removal to one pole, or to cortical substance alone.

E. R. C.

Leegaard, F. Familiær optræden av peritonsillærabsces (angina phlegmonosa). [**Familial occurrence of peritonsillar abscess.**] *Norsk Mag. f. Lægevidensk.*, 1921, **82**, 381–90.

In support of his hypothesis that peritonsillar abscess is more frequent in some families than in others, and that in some cases at least it is due to congenital, predisposing causes, Leegaard has investigated the family histories of 120 patients suffering from peritonsillar abscess. Only in 44 cases could he find no family history of peritonsillar abscess, whereas in the remaining 76 cases there was a history of peritonsillar abscess in one or more relatives. This was obviously an underestimate, for there must assuredly have been many cases of peritonsillar abscess in the patient's family which were overlooked. As a control test, 120 patients not suffering from peritonsillar abscess were questioned as to the occurrence of this disease in their families, and in 110 cases no such family history could be obtained. Of the remaining 10 patients, who gave such a family history, as many as 7 stated that several members of each family had suffered from peritonsillar abscess.

With regard to the question whether recurrence of peritonsillar abscess is due to congenital, predisposing factors, or to conditions acquired at the first attack, Leegaard refers to the possibility of adhesions, formed at a first attack between the palatine arches and the tonsils, being responsible for relapses owing to the retention of secretions. But though such acquired factors may play a certain part, he attaches considerable importance to congenital predisposition, and in support of this view he shows that of the 73 patients who had suffered from peritonsillar abscess three times or oftener, as many as 55 gave a family history of this disease. Of the 17 patients, each of whom had suffered twice from peritonsillar abscess, 8 gave a family history, and of the 23 patients, each of whom had suffered only once, only 8 gave a family history of peritonsillar abscess. In other words, there was a family history in about three-quarters of the cases of recurrent peritonsillar abscess, whereas such a history was obtained only in a third of the patients who had not suffered from this condition more than once. Leegaard suspects that, as in the case of appendicitis, certain families may be more liable than others to contract peritonsillar abscess owing to congenital anatomical factors, such as great length or narrowness of the tonsillar crypts, or peculiarities of the adjoining structures which favour retention of septic material. As in the overwhelming majority of cases of peritonsillar abscess the disease is found near the outer and upper part of the tonsil, it is possible that peritonsillar abscess may be associated with congenitally defective means of drainage from the supratonsillar fossa. The prevention of relapse of peritonsillar abscess by enucleation of the tonsils seems to be confirmatory of this view.

C. L.

Martin, E., Thomas, B. A., and **Moorhead, S. W.** *Genito-urinary Surgery and Venereal Diseases.* Philadelphia and London, J. J. Lippincott, 1920, 12th ed., pp. 927.

The twelfth edition of White and Martin's well-known text-book is substantially the same as the eleventh, with the exception of certain modifications and revisions and the addition of a section on venereal prophylaxis. The treatment of syphilis and gonorrhoea is, on the whole, sound and practical, and many will agree with the authors that a persistently positive Wassermann reaction should not be 'heroically combated at the expense of the patient's health', although their recommendation of mercurial courses in the spring and autumn 'throughout life' in such cases may by some be considered somewhat pessimistic. On the other hand, to regard three injections of arsphenamine given in the primary stage as sufficient treatment, provided the Wassermann reaction remains negative for three years, seems to err on the side of undue optimism. The authors are not convinced of the value of subdural injections in cerebrospinal syphilis; indeed, they think that arsenical treatment may be contra-indicated in widespread cerebrospinal syphilis, and prefer treatment of such conditions with mercury and iodides. With regard to the marriage of syphilitics they are also optimistic, and think that either a man or a woman well treated from the first and with a persistently negative Wassermann reaction may marry in two years; also, that a man with a persistently positive reaction, but no clinical symptoms, is safe after four years, but not so a woman. In the section on hereditary syphilis the question of paternal transmission is ignored, and infection of the foetus is assumed to be always from the mother.

The numerous pathological conditions and abnormalities of the genito-urinary organs and the operations of renal and genito-urinary surgery are described in clear and concise language, assisted by numerous excellent illustrations. The chapters on sexual neurasthenia and sexual perversion are especially sound. C. F. M.

McDonagh, J. E. R. *Venereal Diseases: their Clinical Aspect and Treatment.* London, W. Heinemann, 1920, pp. 419.

In his new book, Mr. McDonagh champions the cause of clinical observation and deplores the widespread public faith in laboratory tests. The time, he says, 'appears to be approaching when every patient will be a test-tube and every doctor an automatic machine.' Too much reliance on laboratory tests, he points out, tends to the neglect of the human side of the patient. As an example of the danger of relying solely upon laboratory diagnosis, he mentions that in 100 consecutive cases of clinically obvious syphilitic chancres, examined by a skilled pathologist, a negative result was returned in no less than 23 cases. Again, in interpreting the Wassermann reaction, he remarks that 'in view of the widespread belief in blood-tests by the public, in whose minds a positive reaction means active syphilis and a negative reaction means a cure', great caution is necessary, and says that he has known of suicides committed by patients as a result of this belief. A persistently positive reaction after adequate treatment, in his opinion, is due to the continued formation of protective substances, and, therefore, best left alone. If this view is correct, which is quite possible, many patients must be over-treated. Mr. McDonagh shares the view held by several other observers—that there has been an increase in neurosyphilis since the introduction of salvarsan, and attributes this increase partly to the too liberal administration of arsenic and mercury, and partly to neglect of the continuation of treatment. He thinks that the toxic effects of arsenic and mercury are due to over-oxidation and that they can be counteracted by reducing reagents, especially by intramuscular injections of intramine—the amino-sulphur compound which he introduced some time ago. To reduce this toxic action of arsenic and mercury he prefers to give them separately. He is not a believer in the intrathecal treatment of cerebrospinal syphilis with salvarsanized serum, and holds that better results can be obtained by intravenous injection of arsenobenzene, followed by simple lumbar puncture. He does not believe that arsenobenzene has any direct spirochaeticidal action, and thinks it acts by increasing the oxidizing action of the patient's protective substances. While Fournier in his long experience failed to establish any relation between different types of chancre and the subsequent course of the disease, Mr. McDonagh believes he can distinguish between chancres which are likely to be followed by mild or by severe syphilis.

In the sections on gonorrhoea Mr. McDonagh severely criticizes some of the modern methods of treatment and thinks that over-instrumentation is to be blamed for many cases of chronic gonorrhoea. In his opinion, the urethroscope is of little value in diagnosis and less in treatment. The rational treatment of gonorrhoea, he says, is by the blood-stream, either by means of chemotherapy or vaccines. Of the chemotherapeutic agents he places most reliance on those which he himself introduced, viz. intramine and trimine (a combination of colloidal manganese, iron, and zinc) and recommends them in chronic gonorrhoea and its complications.

Dealing with the important subject of syphilis and marriage, Mr. McDonagh holds that a time limit is futile, and that we cannot be certain, either by clinical or pathological means, when a patient may marry without risk. He, however, believes that if a man is adequately treated in the primary stage he can marry without risk, especially if his Wassermann reaction is negative before and after a provocative injection of arsenobenzene. Adequate treatment in such cases, in his opinion, consists in four or five injections of arsenobenzene, one injection of intramine, followed by mercury and iodides for a year. When treatment is not commenced till the stage of generalization the risk is much greater.

With regard to the question of gonorrhoea and marriage, Mr. McDonagh concludes that the infectiousness of chronic gonorrhoea has been much overestimated. He has little faith in pathological reports and relies mainly on clinical examination. From the clinical point of view Mr. McDonagh's book is excellent, but his theories on chemotherapy and biochemistry, while highly original, are not always convincing and are stated too dogmatically.

C. F. M.

NEUROLOGY

Bailey, P. The pathology of trigeminal neuralgia. *J. Nerv. & Mental Dis.*, 1921, **54**, 42.

In a paper read before the Boston Society of Psychiatry and Neurology, Bailey reports that histological examination of Gasserian ganglia from numerous cases of trigeminal neuralgia gave negative results, apart from senile changes in cells and interstitial tissue. Therefore the essential lesion must be peripheral. The fact that peripheral section of the nerve-trunks abolishes pain until regeneration has occurred may be taken to confirm this view. Bailey thinks that we must look for pathological changes in the nerve-endings. Clinical observation, such as the initiation of pain by peripheral stimuli, is in accord with such a conclusion. In the discussion following the paper, Cushing expressed the opinion that the character of the pain, its unilateral situation, and the manner of its spread are against its peripheral origin. In a series of nearly 400 cases operated upon by him, pain had recurred on the opposite side in about 4 per cent. Major trigeminal neuralgia might occur in young adults, and therefore there was no foundation for the statement that arteriosclerotic processes in the vessels supplying the ganglion played any part. F. M. R. W.

Mott, F. (1). The psychopathology of puberty and adolescence. The Morison Lectures for 1921. *J. Mental Science*, 1921.

Mott, F. (2). The Second Maudsley Lecture, 1921. *J. Mental Science*, 1921.

In these four lectures are included, among much varied and interesting material, the results of Mott's prolonged and original observations on the morbid lesions in the testis and ovary in both germinal and acquired mental disease. The present abstract refers to this work alone.

In dementia praecox, Mott finds that the *testis* undergoes regressive atrophy, which, according to the duration of the disease, varies from the slightest morphological and biochemical changes to total atrophy of the seminiferous tubules and cessation of spermatogenesis. Speaking generally, he finds that the earlier the onset of symptoms and the longer the duration of life subsequently, the more complete the atrophy. Even the testis of a man of eighty years showed much clearer signs of functional activity. On the other hand, in such an acquired form of mental disease as dementia paralytica, the atrophic changes are focal, and side by side by areas of atrophy are to be seen normal tubules with active spermatogenesis. The *ovary* from cases of dementia praecox shows changes of the same order. To the naked eye the organ is smaller and lighter than normal and has a crinkled appearance. This is true even when the patient has had a child, and they appear rarely to have more than one. Microscopically, there is no evidence of recently matured Graafian follicles. The continuous zone of primordial follicles normally found in early life is absent in this disease. Such small follicles as are present show evidences of degeneration. Such regressive atrophy is not found in dementia paralytica. The critical periods of life as regards mental disease, Mott believes to be adolescence and the climacteric, that is, when the sexual function becomes mature and wanes respectively. He believes this to indicate important relations between sexual functions and mental disease. Discussing the question whether the atrophy of the sexual organs is the cause or an accompaniment of the mental symptoms, he concludes that there is a germinal-biochemical failure of all nuclear material in the body, but of that of the central nervous system and sexual organs particularly, with a corresponding defect of reproductive and 'psycho-physical' energy. This failure in many cases begins before puberty. Turning then to the essential lesion of the nervous system in dementia praecox, Mott concludes, from his own observations and those of Nissl, Alzheimer, and others, that this consists in a parenchymatous degeneration of the neurones, with relatively little morbid change in the mesodermic supporting tissues. The histological peculiarities of the affected neurones are described at length, and Mott concludes that a failure of oxidation processes dependent upon a defect of the vital energy of the nucleus underlies the mental manifestations. A similar failure accounts for the regressive changes seen in the sexual organs.

An admirable series of drawings illustrated the series of lectures.

F. M. R. W.

Souques, M. A., and others. Les Syndroms Parkinsoniens. **[Parkinsonian syndromes.]** *Rev. Neurol.*, 1921, i, 534.

The Paris Society of Neurology chose this subject for discussion at its second annual reunion. The opening paper by Souques covers every aspect of the subject, anatomical, physiological, clinical, pathological, and therapeutic. This paper and the shorter papers following it occupy nearly two hundred pages of the current number of the *Revue Neurologique*, and therefore only the most salient features can be dealt with here. Souques reviewed present anatomical knowledge of the fibre connexions of the corpus striatum, and briefly stated current hypotheses of its functions. His physiological review was entirely non-critical and adds nothing to our knowledge. He concludes that the functions in question are purely motor, and are fourfold. The corpus striatum regulates muscle tone and 'prevents' hypertonus, it maintains muscular repose and thus 'prevents' tremor, and it is responsible for the performance of automatic movements. Finally, it has important vasomotor functions. This is determination of function by what, in a previous review, we have described as symptom-translation, The hypothesis has no experimental support, is not in accord with what we know of tone and automatic movements, and is certainly not physiology. The other contributions to this aspect of the subject were equally disappointing.

Souques discusses the pathological anatomy of paralysis agitans and discards the hypotheses invoking muscular and parathyroid lesions as the essential basis of the disease. He concludes that paralysis agitans is a clinical but not a pathological entity. It may be produced by lesions of different nature involving the corpus striatum, the locus niger, and the subthalamic region. Our knowledge does not yet permit a more precise localization. He believes that the determining causes of Parkinson's disease are uncertain. He rejects emotional disturbances as an important factor, and in this view he was supported by other neurologists present. Trauma, also, he rejects. A far more important determining cause is infection, and the recent epidemics of lethargic encephalitis have brought this factor strongly before us. In many cases arteriosclerosis accounts for the syndrome, while less common are cases in which are found gross lesions in the region of the basal ganglia, multiple softenings, and haemorrhages. He recognizes three clinical forms of the disease; (1) the typical form, with tremor and rigidity, (2) an abortive form with tremor, but without rigidity, and (3) an abortive form with rigidity but no tremor. A further subdivision is into (*a*) pre-senile and senile cases. These are the classic cases, which serve as the descriptive model of the condition. (*b*) Juvenile cases. Here the evolution is more rapid and often the tremor more widespread and violent. There may be a familial or hereditary factor present. (*c*) Presenile syndromes in which the lesion is the status disintegrationis of C. and O. Vogt. (*d*) Cases with gross lesions, and (*e*) post-encephalitic syndromes. Souques believes that we may definitely regard encephalitis lethargica as a cause of paralysis agitans. In most cases, the Parkinsonian syndrome follows ocular palsies with lethargy, and is often a sequel of the mildest cases. It generally develops rapidly, either during the acute illness or not until several weeks after apparent recovery. Rigidity is the predominant symptom, and in the majority of cases there is no tremor. Once established, the syndrome rarely disappears, it remains stationary or slowly progresses.

In respect of the treatment of paralysis agitans, however caused, there appears, from Souque's review, little matter for satisfaction. Organotherapy, principally parathyroid, is commonly futile. Scopolamine and hyoscine give the most striking amelioration of symptoms, but their use is attended with obvious dangers and cannot be indefinitely continued. Arsenical preparations, though advocated by Sicard and others in France, have also been disappointing. Perhaps, least objectionable of all the measures at our disposal are physio-therapeutic, and among these he advocates hydrotherapy and passive movements.

It is not possible to review here the numerous other papers dealing with different aspects of the subject, and the impression left by all of them is that our knowledge of the subject is very incomplete and our remedial measures of inconsiderable value. F. M. R. W.

Buzzard, E. F., and **Greenfield, J. G.** ***Pathology of the nervous system.*** Constable & Co., London, 1921, pp. 334.

It has long been a reproach to neurology in this country that, although it has produced admirable clinical text-books, yet there is no text-book of neuropathology in the language. As far as the student and the general reader are concerned, this omission is most handsomely repaired by the appearance of Buzzard and Greenfield's new book. In their preface the authors insist that 'no student of neurology or of psychiatry can be fully equipped for his work unless he has spent time and energy in a neuropathological laboratory'. The observation might have been made even more general in its application, for, with the ever-widening scope of research, workers in various fields are apt to find themselves faced with neuropathological problems arising in the course of investigations apparently remote in their origin: problems which cannot be satisfactorily resolved without a sound general conception of the ways in which the nervous system reacts to disease in its various forms. In the present number of *Medical Science* we have dealt with one such problem: syphilis of the nervous system is another. Therefore, the book should make an even wider appeal than its authors predicate, for it meets a crying need. That its writers have not alone a wide knowledge of neuropathology, but also a ripe clinical experience, adds considerably to the merit of their book, and among its most valuable features is the section appended to each chapter dealing with the relation of the anatomical to the clinical phenomena. The introductory chapter deals with the general pathology of the nervous system, the reaction of the neuron and of the neuroglia to disease, the paths of infection of the nervous system, and the cerebrospinal fluid. Later chapters are devoted to developmental and familial diseases, injuries, circulatory disturbances, infections and intoxications, syphilis, new growths, and obscure diseases. In two appendices are full details of histological methods and of the modes of investigation of the cerebrospinal fluid. A series of beautifully reproduced photographs illustrates the book, which is a most notable acquisition to neurological literature.

Within the limits of a short review we can refer only to one or two salient features. The chapter on the paths of infection of the nervous system is the best summary of modern knowledge on this subject that we have seen, though there is one statement to which we might take exception; namely, 'that it has long been known' that the toxin of diphtheria reaches the nervous system along the perineural lymphatics. In the period before the war we can recall but a single expression of opinion to this effect, and the view certainly commanded no acceptance, though there is now some evidence that it is correct,

We leave the book with but two regrets; firstly, that the authors have not been more ambitious and have been content with an elementary textbook of less than 400 crown octavo pages; and secondly, that the publishers should have placed so excessive a price upon it. Surely this will restrict its field of usefulness unduly. F. M. R. W.

Jelliffe, S. E. The technique of psycho-analysis. *J. Nerv. & Ment. Dis.*, Monograph Series, No. 26 (Second Edition), 1920, pp. 171.

Although the intention of Dr. Jelliffe seems to have been to provide an introduction to psycho-analysis, the present volume will not be very helpful to the beginner, for it represents a particular view of psycho-analysis considered as a study of the different levels of which the mind is built up. Just as the body recapitulates in each individual the evolutionary history of the race, so does the mind go through its historical stages, and as a fixation of the body at any stage will produce a deformity, such as cleft palate or a branchial cleft, so will a mental fixation produce that kind of deformity known as a psychoneurosis. It is the affair of the psycho-analyst to reveal the 'geological period', so to speak, of the out-cropping symptoms, which should have been integrated and controlled by later mental development. In practice it appears that the Oedipus fixation is the commonest and most important, and by this Dr. Jelliffe does not seem to mean merely gross sexuality towards the parent of the opposite sex, but rather undue prolongation of the normal dependence of the child on the parent. Therefore, in each case the complex is rather a father-mother complex. Some of his examples are quite a revelation; thus, a young man always ate the same food for breakfast—sausages, waffles, and maple sugar. He appears not to have remembered clearly of what his other meals consisted, except that he ate meat of several kinds, and no vegetables but potatoes. His interest in his food, however, lay entirely in this monotonous breakfast—that is, in a diet which was analogous to the monotonous diet of infancy, milk. Therefore, he was still 'hanging on to his mother'. Sausages and waffles are then shown to have associations with the nipples. Q.E.D. The Oedipus situation being grasped by the patient, the difficulties begin, for the management of the transference determines the whole success of the treatment, and both positive and negative transference are extremely dangerous situations, demanding the utmost skill of the physician. When success is obtained, the patient allows his repressions to come freely to the surface and is cured.

The book is like Dr. Jelliffe's other works, full of miscellaneous learning and very difficult to read, and it is too often marred by the most bitter invective against his opponents, especially the 'Janus-faced' who are not entirely opposed to him. Yet he often urges his pupils not to get angry with their opponents. It is curious that there should be so much of this kind of thing in psycho-analytic literature; curious that writers who must surely have been psycho-analysed cannot see the contradiction involved. Their inability to do so must lessen the value of psycho-analysis, for they always insist that resentment against analysis indicates that its opponents are resisting a truth. Is not this equally true of resentment against the criticism of analysis? Dr. Jelliffe says that the best preparation for the beginner is to be analysed by one versed in the business. He also states that at first free associatious are apt to be sticky, and that the analyst must go on pressing the patient until he gets them. It seems to the reviewer that if this pressure be continued firmly enough it would not be difficult to lead the patient up to sexual thought. For example, if a revolver is the symbol, and the patient says that nothing comes into his mind, and is pressed and ultimately says that it is a hollow tube which discharges something from a magazine with great heat, it is but a short step to the physiological analogy. We have here created a sexual symbol which had never really existed before, and henceforth sexual symbolism comes easy to the patient. As all the present writers on psycho-analysis have been analysed either by Freud himself, or by those in apostolic succession to Freud, the universality of these symbols would be no criterion of their truth; in short, they would be simply Freud's private symbols. Therefore one questions whether an analysis at the hands of one of the orthodox analysts has the value constantly claimed for it. Dr. Jelliffe gives at the outset a valuable list of those who should not be analysed, amongst whom it is interesting to find hysterical young girls, because of the danger of too strong transference. The warning seems salutary. T. A. R.

PATHOLOGY AND BACTERIOLOGY

Gillespie, L. J. Color standards for the colorimetric measurement of H-ion concentration. *J. Bact.*, 1921, **6**, 399.

This paper is a criticism of a previous paper by Medalia (*Medical Science*, 1920–1, **3**, p. 555). This latter investigator has presented a system of colour standards which resembles one published by the present author. The proposed tables of Medalia are in serious disagreement with the results of Gillespie, who finds that the conflict of observations lies in the plan followed by Medalia. The author goes into technical details to show why Medalia is in error. He then proceeds to describe an instrument for further study of indicator constants and behaviour which was devised too late to be of service in his previous paper. It is a colorimeter for two-coloured indicators. The optical assumptions which underlie its use are shown to be practically the same as those upon which ordinary colorimetry is based.

W. A. M. S.

Florence, Laura. Spiral bodies in bacterial cultures. *J. Bact.*, 1921, **6**, 371.

The authoress draws attention to the occurrence and nature of spiral bodies which were originally found by Loeffler, in 1889, when staining the flagella of typhoid bacilli and potato bacilli. They were afterwards studied and beautifully photographed in 1894 by R. Pfeiffer in specimens made by Novy. Although mostly found in anaerobic cultures the present writer has found them in cultures of aerobes, especially in the condensation water. They have been mistaken for spirochaetes, but may be distinguished by (1) their lack of motility, (2) by their reaction towards stains, and (3) by the impossibility of obtaining them in pure culture. They only occur in motile cultures and disintegrate in sterile water. W. B.

Malone, R. H., and **Goré, S. N. The detection of indole in bacterial cultures. A criticism of various methods of applying the nitroso-indole and rosindole reactions, based on a comparative study of their delicacy and specificity.** *Indian J. M. Research*, 1921, **8**, 490.

Goré, S. N. The cotton-wool plug test for indole. A new technique of applying Ehrlich's reaction for detecting indole in bacterial cultures. *Indian J. M. Research*, 1921, **8**, 505.

In the first paper the authors give a short account of the comparative value of tests for indol and point out that neither the nitroso-indol nor the rosindol reaction are specific for indol although the latter is the more delicate. The inconsistent results obtained by workers may be attributed to (*a*) the absence of tryptophane or a tryptophane polypeptide group from the culture media employed, (*b*) the presence of degradation products of tryptophane, other than indol, and (*c*) defective means of applying the test. They consider that the best technical method is that which they call 'Goré's cotton-wool plug test', which is described by Goré as follows: (1) Remove the plug of the culture-tube and if it does not already consist of white absorbent cotton-wool, cover its under surface either with a thin layer of such wool or with a piece of filter-paper; (2) moisten evenly the under surface of the plug first with a few drops of persulphate of potassium solution (1 per cent.) and then with a few drops of para-dimethyl-amido-benzaldehyde solution; (3) replace the treated plug and push it down until it is about an inch above the surface of the broth culture; (4) place the prepared culture-tube upright in the gently boiling water-bath; (5) allow the heat to act for about 15 minutes. The plug is removed and examined in a good light, when, if indol is present, the under surface of the plug becomes of a rose colour owing to the action of the volatilized indol. W. B.

Andrewes, F. W., and Neave, S. The nature and systematic position of *B. paratyphosus* C. [E.] *Brit. J. Exper. Pathol.*, 1921, **2**, 157.

(1) A new form of paratyphoid fever has been observed during the war by many investigators, chiefly in Eastern Europe and in Asia. The causal organism, *B. paratyphosus* C, is distinct from *B. paratyphosus* A and B, though presenting relationship to the latter. (2) In this paper there is described a case of paratyphoid C occurring in England. The bacillus isolated is compared with other members of the Salmonella group in detail. (3) In its cultural and fermentative characters *B. paratyphosus* C is shown to differ from *B. paratyphosus* B in its failure to ferment inosite and in its slower rate of alkali production. It differs from *B. suipestifer* in fermenting arabinose and dulcite. (4) A short review is given of the serological properties of *B. suipestifer* and of the related forms *B. voldagsen* and *B. glässer.* The suipestifers fall into two serological groups, sharply separable by certain sera. By absorption tests it is shown that a Group I suipestifer will exhaust the sera of both Groups I and II, but that a Group II suipestifer will exhaust only Group II sera, leaving the specific titre of Group I sera untouched. (5) *B. paratyphosus* C is shown to belong serologically to the Group I suipestifers, in spite of the divergence in cultural characters. (6) Different strains of *B. paratyphosus* C vary in their relation to *B. paratyphosus* B. In some the B element is absent, in others very obvious. An example of each variety was isolated from the case described, and it is shown that the strain which at first showed no relation to *B. paratyphosus* B gradually underwent a serological change, acquiring the property of being partially agglutinated by a paratyphoid B serum. P. F.

Chesney, A. M. An immunologic study of *Bacillus influenzae*. *J. Infect. Dis.*, 1921, **29**, 132.

The purpose of this research was to determine the immunological relationship of strains of *B. influenzae* obtained from adults during the course of an attack of influenza. Twelve strains were studied. Cross-agglutination tests and absorption experiments indicated that four of them were identical. No evidence of relationship to strains obtained from another source was encountered. The author considers that the influenza bacillus is a representative of a heterogeneous group of haemoglobinophilic bacteria. Among themselves they differ in their antigenic properties although immunologically identical strains may occur in the same patient. The results lend no support to the view that the influenza bacillus is the cause of epidemic influenza. W. B.

Yabe, S. Grouping of influenza bacilli. *Brit. J. Exper. Pathol.*, 1921, **2**, 197.

(1) Influenza bacilli can be divided definitely into two groups according to the character of indol formation. Out of 29 strains examined, 18 strains (62 per cent.) form indol. No intermediate strains are found. It is very probable that this character of indol formation is not alterable by prolonged subculture. (2) By morphological and immunological study it is impossible to divide influenza bacilli into groups, because there are found as many intermediate strains as there are strains examined. P. F.

Davis, D. J. (1). Food accessory factors in bacterial growth. III. Further observations on the growth of Pfeiffer's bacillus (*B. influenzae*). *J. Infect. Dis.*, 1921, **29**, 171.

Davis, D. J. (2). The accessory factors in bacterial growth. IV. The 'satellite' or symbiosis phenomenon of Pfeiffer's bacillus (*B. Influenzae*). *J. Infect. Dis.*, 1921, **29**, 178.

Davis, D. J. (3). The accessory factors in bacterial growth. V. The value of the satellite (or symbiosis) phenomenon for the classification of hemophilic bacteria. *J. Infect. Dis.*, 1921, **29**, 187.

In a previous paper the author emphasized the importance of two substances in the growth of *B. influenzae*, one being haemoglobin or a derivative while the other was obtainable from plant tissues (carrot, potato), animal tissue, bacteria, yeasts, &c. The first of the present three papers carries the subject farther, the author showing that blood media heated to 60° C. or higher, for definite periods of time yield profuse cultures of influenza bacilli. Blood media heated to 120° C. for a few minutes in the autoclave are rendered incapable of supporting growth, although the inactive superheated blood medium may be reactivated by adding to it plant, animal, and bacterial extracts which by themselves do not support the growth of influenza bacilli. The latter substances also lose their supporting property if exposed to a temperature of 120° C. for a few minutes. The author considers that the growth process of the influenza bacillus may be represented thus: plain medium + heat resistant substance (haematin or derivative) + thermolabile substance = growth of *B. influenzae*.

In the second paper the phenomenon of 'satellism' as observed in connexion with Pfeiffer's bacillus is described in detail. It is observed in association with bacteria yeasts and fungi of various kinds and their filtrates, also with plant and animal tissues and their extracts and filtrates. Heating in the autoclave for 30 minutes destroys the activities of these substances. *B. influenzae* will not grow on clarified autoclaved blood medium. Neither will it grow on plain medium to which micro-organisms or tissues or their filtrates (haemoglobin free) are added. When, on the other hand, the two factors are mixed a good growth results, from which the author infers that diffusible products or extracts of bacteria, fungi, tissues, &c., stimulate the growth of *B. influenzae* in conjunction with haematin or with haemoglobin. Thus profuse growth of influenza bacilli occurs in the immediate neighbourhood of colonies of microbes or pieces of animal or vegetable tissue.

In the third paper the author emphasizes the importance of 'satellism' for the purpose of classification and identification of haemophilic bacteria. The author has tested many hundreds of strains of influenza bacilli and has invariably found that they show the satellite phenomenon when grown with another organism on blood plates. On the other hand, the influenza bacillus will not favourably influence itself, although it will be favourably influenced by other haemophilic bacteria such as *B. pertussis* Bordet, Morax-Axenfeld bacillus, and Koch-Weeks's bacillus. W. B.

Tongs, M. S. The effects of hemolytic streptococci on the blood and hemopoietic organs of rabbits. *J. Infect. Dis.*, 1921, **29**, 141.

The author undertook his experiments in order to throw light on the changes produced on the blood and haemopoietic organs of rabbits by haemolytic streptococci of the beta type. The animals were injected intravenously and blood counts were made at varying intervals. After death the haemopoietic organs were examined histologically. The results showed that haemolytic streptococci may produce a toxic substance which causes degeneration of leucocytes and marrow-cells *in vitro*. Intravenous injections of cultures are followed by regressive changes in the amphophile leucocytes in the peripheral circulation and in the marrow-cells. It is this degeneration which gives rise to leucopenia. When of low virulence, haemolytic streptococci produce no changes of a retrograde character but cause a disarrangement of the Arneth index to the left. There may be a gelatinous degeneration of the bone-marrow and hyperplasia of phagocytic cells in the spleen. By small doses of non-virulent haemolytic streptococci a secondary anaemia may take place. W. B.

Lord, F. T., and **Nye, R. N.** (1). **Studies on the pneumonic exudate. I. Effect of preservation, temperature, dialysis and salt concentration on the enzyme in the pneumonic lung.** *J. Exper. M.*, 1921, **34**, 199.

Lord, F. T., and **Nye, R. N.** (2). **Studies on the pneumonic exudate. II. The presence of enzyme and anti-enzyme in the pneumonic lung. Local ferment-antiferment balance.** *J. Exper. M.*, 1921, **34**, 201.

Lord, F. T., and **Nye, R. N.** (3). **Studies on the pneumonic exudate. III. The presence in the pneumonic exudate of a large amount of specific antigen.** *J. Exper. M.*, 1921, **34**, 207.

Lord, F. T., and **Nye, R. N.** (4). **Studies on the pneumonic exudate. IV. The presence in the pneumonic lung of a soluble substance inhibiting agglutination by the homologous serum.** *J. Exper. M.*, 1921, **34**, 211.

One of the authors (Lord) previously reported (1919) the existence in cellular material obtained from pneumonic lungs of a proteolytic enzyme which was able to erode the surface of Loeffler's serum at hydrogen-ion concentrations of 7·3 to 6·7. In the first of present series of conjoint reports it is shown that the enzyme was still active after 18 months' preservation. It was active at incubator treatment before and after heating to 65° C. for 1 hour, and was slightly active at room temperature. It was inactivated by heat at 75° C. for 1 hour. Dialysis of the enzyme could not be demonstrated, and it was found that it was active after being mixed with strong concentrations of sodium chloride. In the second communication experiments are given which indicate that purulent sputum obtained during life and the exudate at autopsy from the later stages of lobar pneumonia commonly erode the surface of Loeffler's serum. Cellular material obtained from pneumonic lung in an early stage of lobar pneumonia failed to erode the surface of serum until washed with normal saline.

The third paper brings evidence to show that in lobar pneumonia due to fixed types of pneumococci a specific precipitin reaction is obtained when the pneumonic exudate is mixed with homologous antipneumococcic serum. In the fourth paper experiments are detailed which go to show that specific agglutinins for homologous pneumococci are absent or present only in small quantity in the pneumonic exudates due to fixed types of pneumococci. Apparently the pneumonic lung contains a soluble substance inhibiting agglutination of the fixed types of pneumococci by homologous antipneumococcus serum. W. B.

Cecil, Russell L., and **Steffen, G. I. Studies on pneumococcus immunity. I. Active immunization of monkeys against pneumococcus Type I pneumonia with pneumococcus Type I vaccine.** *J. Exper. M.*, 1921, **34**, 245.

An analysis has already been given of the extended researches of Blake and Cecil on experimental pneumonia (*Medical Science*, 1920–1, **3**, 63). In one of their investigations the protective power of subcutaneous doses of pneumococcus Type I vaccine was studied, and it was found that when these doses were comparable to those used in man protection against accidental or intentional infections with pneumococcus Type I did not ensue although the course of the disease was apparently modified. The present paper deals with experiments in which larger doses of pneumococcus vaccine were employed on three species of monkeys, viz. *Macacus rhesus, M. syrichtus*, and *Cebus capucinus*. Of these *M. rhesus* is the least susceptible. When three large doses of vaccine are injected subcutaneously, subsequent immunity was complete even after intratracheal insufflation of pneumococci of maximal virulence. The doses employed were 20, 40, and 60 billion cocci respectively at relatively short intervals. Although not expressly stated, it is to be presumed that the word 'billion' employed is that of the U.S.A., viz. 1,000 million. It was also found that intravenous inoculation of small doses (400–1,600 million cocci) also confers complete immunity against the homologous type of pneumococcus. An examination of the sera of the protected animals indicated that specific protective substances may or may not be present, and that there appears to be no intimate relation between active immunity against pneumonia and the presence or absence of protective substances in the serum of the vaccinated animal. Thus two specimens of *Cebus capucinus* which had been vaccinated subcutaneously withstood without symptoms an intratracheal dose of pneumococcus which killed a control on the third day with an overwhelming septicaemia. Blood taken from the two vaccinated animals just before the intratracheal test dose failed to protect mice against the homologous pneumococcus. The intravenous administration of pneumococcus vaccine was believed to induce a higher degree of immunity than the subcutaneous injection. W. B.

Kahn, R. L. Studies on complement fixation. I. The rate of fixation of complement at different temperatures. *J. Exper. M.*, 1921, **34**, 217.

The plan of this research was (1) to establish the presence of specific complement-fixing antibodies in the sera of rabbits previously immunized with specific proteins, and (2) to determine the rate of fixation of complement and to what extent it is affected at different temperatures. The antigens employed were edestin (from hemp-seed) and phaseolin (from kidney beans), and the temperatures of fixation studied were 8–12° C., 18–23° C., and 37·5° C. respectively. Tables and curves are presented to show that the rate of fixation of complement is determined by the concentration of antibodies in the immune serum, that the greater part of the fixation of complement takes place during the first hour, and that at ice-box temperature fixation is practically completed at the end of four hours. It is further shown that the rate of fixation is practically the same at ice-box, room, and warm bath temperatures, the tendency being for slightly stronger fixation at ice-box temperature. W. B.

Westergren, A. **Studies of the suspension stability of the blood in pulmonary tuberculosis.** *Acta Med. Scand.*, 1921, **54**, 247–81.

Westergren has studied the rate of sedimentation of the cells of citrated blood in a vertical glass pipette of about 1 c.cm. capacity and a height of 200 mm. He made about 3,000 examinations on about 500 persons, many of whom were male consumptives in a Swedish hospital for tuberculosis. He found that in health, apart from pregnancy, the rate of sedimentation was about 2 mm. per hour; when it was 10 mm. or more, it was definitely pathological. In some cases it was as great as 120 mm. per hour. In the diagnosis of tuberculosis the value of this test was greatly reduced by the rate of sedimentation being much increased by various other diseases. But though the test was not specific it proved a valuable guide to the degree of activity of the tuberculosis, and it proved more reliable than the patient's temperature. Thus, the rate of sedimentation was not only increased by fever, but even before the temperature began to rise an increase was noted in several cases. Westergren found that sources of error in this test were comparatively insignificant, but he admits that the relative number of blood-cells in each case may possibly determine the rate of their sedimentation to a certain extent. C. L.

Cramer, H. Über die neue Tuberkulosewelle nebst einem Beitrag zum jetzigen Stand der Tonsillartuberkulose. [**The new tuberculosis wave and the present position of tonsillar tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1921, **46**, 307–41.

Schulz, E. Tonsillitis chron. als Ursache einer Mischinfektion bei einem Fall von Lungentuberkulose. [**Chronic tonsillitis the cause of a mixed infection in a case of pulmonary tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1921, **47**, 1–5.

Cramer has examined for signs of tuberculosis the tonsils of 38 patients suffering from advanced pulmonary tuberculosis, and in all but 2 cases he has found these signs. They were also demonstrable in 8 out of 15 cases of non-ulcerating pulmonary tuberculosis. In 9 cases of tuberculosis not involving the lungs there were 3 showing tuberculosis of the tonsils. In 48 cases without macroscopic signs of active tuberculosis there were 6 showing primary tuberculosis of the tonsils. But this was found only once among 34 cases in which hypertrophic tonsils had been removed. Comparing his figures with those of other observers, Cramer notes that his show a marked rise in the incidence of tuberculosis of the tonsils as indicated by epithelioid tubercles with or without giant cells. In most of his positive cases these tubercles were strictly localized and were of more or less recent origin. He regards his findings as further proof of the lowered resistance to tuberculosis demonstrable in Germany in recent years.

Schulz records a case of chronic pulmonary tuberculosis in a man of 40, whose sputum contained numerous staphylococci and influenza bacilli as well as tubercle bacilli. The flora of the tonsils included diplococci, Friedlaender's bacilli, staphylococci, and a few rods suggestive of diphtheria bacilli. The instructive and suggestive feature of this case was the disappearance of cocci from the sputum, the return of the temperature to normal, and the cessation of other clinical signs of a mixed infection after tonsillectomy. The case suggests that the mixed infection of pulmonary tuberculosis may, in a certain proportion of cases, be traced to a primary focus in the tonsils, and may be eradicated by their removal. C. L.

Pfeiffer, Robert, und **Robitschek, W.** Ein neues Tuberkelbazillenanreicherungsverfahren mit Mastixemulsion. [**A new method of enrichment for tubercle bacilli by means of a mastic emulsion.**] *Centralbl. f. Bakteriol.* (&c.), 1921, **87** (Orig.), 27.

The authors add one more to the long list of methods which have already been devised for concentrating tubercle bacilli in sputa or other fluids. The novelty of their method consists in the use of an alcoholic solution of mastic blown into water. A 10 per cent. solution of mastic is first made in absolute alcohol, and for use 0·5 c.cm. of this stock solution is diluted with 4·5 c.cm. absolute alcohol, and is blown into water by means of a pipette. For the actual examination of sputum or other fluid suspected to contain T.B., 50 c.cm. are mixed with three times the volume of water in an Erlenmeyer's flask which is placed in a water-bath and heated for about half an hour. 8 c.cm. of the homogenized sputum is mixed with 2 c.cm. of the diluted mastic solution in a sedimenting tube and the mixture is left for 24 hours, after which it is centrifuged, the deposit, a whitish granular mass, being then spread on slides which are stained by Ziehl-Neelsen or other method. The results are claimed to surpass those obtained by any other technique. W. B.

Bernblum, W. Vergleichende Untersuchungen der von Ziehl-Neelsen, Gasis-Telemann, Kronberger, Unna-Pappenheim und Konrich angegebenen Färbemethoden zum Nachweis von Tuberkelbacillen. [**Comparative examination of the methods for staining tubercle bacilli devised by Ziehl-Neelsen, Gasis-Telemann, Kronberger, Unna-Pappenheim, and Konrich.**] *Centralbl. f. Bakteriol.* (&c.), 1921, **87** (Orig.), 23.

The author carried out comparative examinations on 400 specimens of sputa by the methods devised by Ziehl-Neelsen, Gasis-Telemann, Kronberger, Unna-Pappenheim, and Konrich. Two preparations of each sample of sputum were examined by each method, and the tubercle bacilli found were enumerated in twenty-five microscopic fields. The conclusion reached was that by Konrich's method more tubercle bacilli were found in almost all the preparations than was the case with any of the other methods. The method of Konrich consists in staining with hot carbol-fuchsin for ½ to 2 minutes; thorough washing in water; decolorization in 10 per cent. sodium-sulphite solution; washing in water; counterstaining for ¼ to ½ minute with watery solution of malachite green (sat. aqueous sol. of malachite green 50 + 100 water). W. B.

Lange, L. Ueber das Friedmannsche Tuberkulose-Schutz-und-Heilmittel. I. Literarisch-kritische und experimentelle Untersuchungen über den Friedmannschen Heil- und Schutzimpfstoff gegen die Tuberculose. [B.] [**On Friedmann's tuberculosis 'cure'. I. Literary, critical, and experimental researches on Friedmann's curative and protective vaccine for tuberculosis.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **32** (Orig.), 230–324.

For the last 18 years the medical world, especially on the Continent, has been in a state of constant turmoil with respect to the origin and value of the cultures recommended by F. F. Friedmann for the cure of tuberculosis, and latterly great press campaigns, both for and against the so-called 'cure', have been organized in Germany. From a scientific point of view many have entered the field and the literature is extensive and complex. The author of the present paper has made it his business to analyse all the bibliographical output and at the same time to carry out experiments of his own which would bring the problem to a definite solution. This he seems to have succeeded in doing in a very exact manner and without obvious partizanship. He makes it perfectly clear that Friedmann's 'cure' has varied from time to time in constitution, and has been composed of at least three different strains of acid-fast bacilli. The first was isolated in 1902 from two turtles (*Chelone corticata*) which died of tubercle in the Berlin Aquarium. As they were not in contact with each other it was assumed and stated that they must have been infected separately from a keeper who at the time was suffering from pulmonary tuberculosis. Friedmann believed that the human tubercle bacilli had undergone a wonderful process of attenuation in the body of the turtle—an attenuation which rendered it harmless for man while at the same time effecting a cure of even the most advanced cases of pulmonary consumption. It was with this culture that Friedmann unsuccessfully attempted cures in America and Canada after a widespread press campaign had prepared the way for his visit to the western hemisphere. In 1904 it was elicited from him that at that time he was employing another turtle strain, but nothing was now said with reference to any connexion with human T.B. A third strain was obtained from a tortoise (*Testudo graeca*) in 1906, although its source was first given by Friedmann in 1914. From his own experiments the present author finds that in very large doses Friedmann's culture is non-pathogenic for guinea-pigs and rabbits, and in general he considers that Friedmann's cultures are much more closely allied to the ordinary strains from cold-blooded animals than to true tubercle bacilli. There are no grounds for supposing that Friedmann's cultures are more pathogenic for human beings than are other saprophytic acid-fast bacteria. W. B.

Selter, H. Ueber das Wesen der Tuberkulinreaktion. [**On the nature of the tuberculin reaction.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **32** (Orig.), 325.

The author finds that neither filtrates nor emulsions of tuberculous organs when mixed with old tuberculin and guinea-pig complement produce a reaction in healthy guinea-pigs. This would indicate that a poison is not produced by the combination of tuberculous tissue and tuberculin, as has been frequently supposed. The reaction produced by injection of tuberculin in tuberculous animals is not, according to the author, of an anaphylactic character. Sublethal doses of tuberculin produce no protective properties—in other words, tuberculin, according to the author, is not antigenic. It is not possible to transmit the tuberculin susceptibility in a passive manner. Tuberculin susceptibility is brought about only by living tubercle bacilli, but not by those which have been killed, although the latter may induce a tuberculous protein anaphylaxis. The author considers that tuberculin susceptibility corresponds to tuberculous protection, in that freshly introduced tubercle bacilli induce a specific form of inflammation which leads to the destruction of the bacilli. Tuberculin sensitivity or allergy is therefore a defensive mechanism. W. B.

Dernby, K. G., and **Blanc, J.** **On the growth and the proteolytic enzymes of certain anaerobes.** *J. Bact.*, 1921, **6**, 419.

In this paper the authors have determined the relation between growth and hydrogen-ion concentration for a certain number of anaerobes, notably

B. sporogenes, *B. histolyticus*, *B. putrificus*, and *B. welchii*. They have also studied the proteolytic activity of filtrates of *B. sporogenes* and *B. histolyticus*. They find that the hydrogen-ion concentrations for the growth of these anaerobes have the limits P_H 5 to P_H 9, the optimal range for all of them being at or about the neutral point P_H 7. The proteolytic activity of filtrates of *B. sporogenes* and *B. histolyticus* is believed to be due to a tryptase. Gelatin is liquefied and peptone disintegrated in the range P_H 4 to P_H 8, the optimum reaction for both reactions being about P_H 6.

W. B.

Wilcox, Harriet L. The effect of pepton upon the production of tetanus toxin. *J. Bact.*, 1921, **6**, 407.

The authoress has made a comparative study of the influence of various peptones in the production of tetanus toxin. Before the war potent toxin was generally obtained when Witte's peptone was used. As the supply, however, came to an end, many other 'peptones' were put on the market, with the result that the toxin yield of tetanus cultures was insufficient or variable. By comparative tests the authoress finds that 'Berna' peptone can be used as a substitute for Witte's product. This Berna peptone was put on the market by the Swiss Vaccine and Serum Company of Berne, and was stated to be made according to Witte's recipe. It may, however, have actually been Witte's peptone in disguise. In any case it was only with these two products that a toxicity of 1 : 100,000 could be obtained.

W. B.

Semerak, C. B. Changes in the human central nervous system in botulism. *J. Infect. Dis.*, 1921, **29**, 190.

An account of the changes in the central nervous system of a girl aged 17 who died with symptoms suggestive of, but not definitely proved to be, botulismus. In favour of the diagnosis were the facts that several persons were affected after consuming the same smoked ham and salted pork, the similarity of the clinical course and symptoms and their correspondence with changes in the central nervous system, the exclusion of trichinosis, or ptomaine poisoning, and also the fact that the lesions did not correspond to epidemic encephalitis or to other known forms of the disease. The lesions were confined to the vascular system of the central nervous system, thrombosis in arteries and veins being the initial change, followed by ischaemic necrosis, and later by inflammation. According to the author the poison had no direct action on the nerve-cells, the regressive changes being secondary and due to disturbances in the blood-supply. The ganglion cells of origin of the motor cranial nerves are always involved because their blood-supply comes from terminals of branches of the vertebral arteries, which appear to be the seat of predilection of the thrombosis.

W. B.

Reddish, G. F. An investigation into the purity of American strains of *Bacillus botulinus*. *J. Infect. Dis.*, 1921, **29**, 120.

The author points out that the descriptions of *Bacillus botulinus* by various workers in the United States differ markedly in certain respects from those of van Ermengem and other European investigators, and he proceeds to show that non-toxic strains were isolated by him from 18 out of 19 so-called strains of *B. botulinus*, the non-toxic cultures being undoubtedly *B. sporogenes*. He thinks that the unsatisfactory results of sero-therapy of botulismus may be attributed to the fact that impure cultures have been employed in the immunization, the toxicity of the cultures varying with age and with the degree of contamination. W. B.

Davis, D. J., and **Matthews, S. A. The bacteriology of the blood of dogs with Eck fistula.** *J. Infect. Dis.*, 1921, **29**, 313.

Micro-organisms are believed to pass from the bowel into the portal branches, being carried thence to the liver, where they are destroyed by some protecting mechanism. The authors have tested this belief upon dogs on which an Eck fistula had been established. It is needless to say that an Eck fistula is an artificial communication between the portal vein and the vena cava with subsequent ligation of the portal vein at the hilum of the liver just above the anastomosis. In this way the liver is excluded from the portal circulation and receives its entire blood-supply from the hepatic artery. The authors established Eck's fistulae in a number of dogs and then examined the blood for bacteria which presumably passed from the bowel into the circulation directly. The experiments did not indicate that many bacteria had been able to gain access to the blood. Further, bacteria disappeared as quickly from the blood of dogs with Eck's fistulae as in normal animals. It is also stated that after an experience of about 100 dogs with Eck's fistulae there was no evidence that the animals were more prone to infection than normal dogs, although some of the animals operated upon survived up to three years. W. B.

Kodama, R. The antibodies for sheep blood and complement of the aqueous humor in normal and immunized rabbits. *J. Infect. Dis.*, 1921, **29**, 171.

This is a study of the antibodies and complement of the aqueous humor of the rabbit in normal and immunized conditions, the results showing that the serum of normal rabbits contains lysin and opsonin, also agglutinin in small quantity for sheep's corpuscles, but no precipitin for sheep's serum. The aqueous humor of normal rabbits contains a small amount of opsonin and lysin for sheep's corpuscles, but no agglutinin or complement, and no precipitin for sheep's serum. On immunization with sheep's erythrocytes the antibodies mentioned appear in the blood, although the aqueous humor gives an increase in lysin and opsonin only, remaining destitute of other antibodies. When the aqueous humor is withdrawn with care the new fluid which accumulates has a far greater amount of antibodies in it than the original fluid, but this enhanced content does not last longer than 24 hours.

W. B.

Russ, V. K., und **Kirschner, L.** Experimentelle Studien über die Funktion der Milz bei der Agglutininproduktion. [**Experimental studies on the function of the spleen in the production of agglutinins.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **32** (Orig.), 113.

A series of experiments is described in which splenectomized were compared with normal rabbits with regard to their capacity of producing antibodies, especially agglutinins. According to the authors, removal of the spleen ten days before the injection of an agglutinogen causes a delay in the appearance of agglutinin in the blood-serum. A subsequent agglutinogenic injection causes a more rapid increase in the agglutinin content than is the case with animals which still possess their spleens. The authors believe that the spleen plays an important part in the formation of agglutinins, although this function can be taken over by other organs. Splenectomy carried out on animals already immunized brings about a great diminution in the antibody content in the serum, which diminution appears to be independent of the mere shock from the operation. A rise in the agglutinin content of the serum from artificial hyperthermy (from deutero-albumose, milk, or staphylococcic injections) does not take place in splenectomized rabbits. W. B.

Douglas, S. R., and **Fleming, A.** **On the antigenic properties of acetone-extracted bacteria.** *Brit. J. Exper. Pathol.*, 1921, **2**, 131.

(1) Acetone-extracted bacilli are a form of bacilli convenient for storage and apparently keep their antigenic properties unchanged indefinitely. (2) They are very easily dissolved by tryptic and other proteolytic ferments. (3) When employed as vaccines, acetone-extracted bacilli appear to have antigenic properties fully as great as vaccines made by other methods. (4) They also form a very suitable antigen for use in complement-fixation tests. (5) Suspensions of these extracted bacilli are agglutinated by immune sera only after a long period and by dilutions more concentrated than is the case with suspensions of living or formolized bacilli. (6) Preliminary experiments appear to show that acetone-extracted bacilli which have been digested with trypsin when injected into animals produce a marked increase (equal to or greater than undigested bacilli) of the bactericidal power, but the increase of the agglutinating power is very much less marked. The extraction by acetone is carried out as follows: the bacteria are washed up with a minumum of saline and this is thrown into excess of acetone. After 24 hours the precipitated bacteria are collected into a Soxhlet thimble and extracted with acetone for 40 hours. The dried remnant is the acetone-extracted preparation. P. F.

Douglas, S. R. **On some characters of the cleavage products of certain bacteria, with special reference to their toxicity and antigenic properties.** *Brit. J. Exper. Pathol.*, 1921, **2**, 175.

Emulsions of acetone-extracted bacteria which have been digested with trypsin for a suitable period have a toxicity which is the same as, or at times greater than, that of emulsions of untreated bacteria of equal density. The toxin present in the tryptic digests is the specific bacterial endotoxin which is usually produced in the body by the lytic action of the body-fluids. Antitoxin prepared by the injection of untreated bacteria completely neutralizes the toxic properties of the tryptic digests. When bacterial digests are injected into animals the bactericidal and precipitating powers are greatly increased. Antitoxin is also formed, but there is no increase of either the agglutinating or opsonic powers. This shows that the agglutinating and precipitating properties of the serum, instead of being very closely related or even identical, are quite distinct from one another. It is also suggested that the antigens giving rise to the agglutinating and opsonic powers are produced during the very early stages of the solution of the bacteria by the body-fluids, while the antigens, in response to which the body produces the bactericidal, antitoxic, and precipitating powers, are formed during a comparatively late period of the lytic process. Repeated injections of untreated bacteria cause diminution of the lytic power of the body-fluids even when comparatively small doses are employed. This would account for the difficulty in producing potent anti-endotoxic sera, as the loss of the lytic power would prevent the injected bacteria being digested *in vivo* as far as the toxic phase, and, in consequence, no antitoxic response would be evoked. Digestion of the bacteria *in vitro* presents the endotoxin preformed to the body, and so may lead to the production of much more potent antitoxic sera. Digests of bacteria should prove to be more suitable for testing the potency of anti-endotoxic sera than emulsions of untreated bacteria, and since such digests contain large amounts of the specific precipitable substance they should be employed in estimating the precipitating properties of sera. Other purposes for which such digests may be employed are: (i) As antigens in complement-fixation tests; here it is suggested that the activity of a disease might be recognized by the detection in the blood of antibodies to particular products of bacterial cleavage by using as the antigen the corresponding phase of a tryptic digest. (ii) As vaccines for therapeutic use, especially in those cases which have become tolerant to the ordinary vaccine—a condition in which the body appears to have lost all power of breaking down the bacteria of the vaccine. P. F.

Wells, H. G., and **Osborne, T. B.** **Anaphylaxis reactions with purified proteins from milk.** [**B.**] *J. Infect. Dis.*, 1921, **29**, 200.

This paper deals with the chemical and immunological differences which are found to be present in the proteins of milk. Chemically there is evidence of the existence of four distinguishable proteins: (1) casein, characterized by a high phosphorus content; (2) lactalbumin, a water-soluble protein which contains no phosphorus; (3) lactoglobulin which contains 0·24 per cent. of phosphorus; and (4) an alcohol-soluble protein recently described by Osborne and Wakeman (1918). The anaphylactic experiments were made on guinea-pigs raised on a diet which did not contain the proteins under investigation, and every possible precaution was taken to avoid contamination, especially of the sensitizing doses, with even the smallest possible quantity of the protein to be used for the intoxicating dose. The results of nearly 200 experiments are set out in tabular form, which go to confirm the view that by the anaphylaxis test it can be shown that the four proteins in milk are immunologically distinct. Of these proteins only one, the globulin, sensitizes to ox serum or causes reactions in animals sensitized to ox serum. Casein is not so active as some other soluble proteins in producing sensitization and shock, although its activity is by no means low. Lactalbumin and casein are entirely distinct chemically and immunologically, and the same is true of lactalbumin and the alcohol-soluble protein. The authors believe that immunological methods are a great aid, and in many cases indispensable in preparing proteins in a state of purity, and may be used to furnish information concerning chemical relations of proteins from different sources. W. B.

MacNalty, A. S. The morbid histology, bacteriology, and experimental pathology of encephalitis lethargica. [**B.**] *Brit. J. Exper. Pathol.*, 1921, **2**, 141.

This paper contains a detailed critical review of the subjects mentioned in the title, with particular reference to the differences between encephalitis lethargica and other clinically similar diseases. P. F.

Brown, W. H., and **Pearce, Louise. Note on the preservation of stock strains of *Treponema pallidum* and on the demonstration of infection in rabbits.** *J. Exper. M.*, 1921, **34**, 185.

Hitherto it has been supposed that infections of rabbits with *Treponema pallidum* were self-limiting and that with the healing of the lesions the infection became extinct. The authors have carried out test inoculations with material from inguinal or popliteal glands of 51 infected rabbits, and have obtained positive results in all cases. The material included four classes of animals. (1) Those with developing or active infections of from 48 hours to 2½ years' duration; (2) animals with latent infection in which no lesion had been present for 3 months to 2 years with a period of infection ranging from 7 months to 4 years and 3 months; (3) drug-treated animals in which no lesions had recurred during 3 months; (4) animals used for serial passage of *T. pallidum* from lymph node to testicle over a period of about 14 months. With old strains of *T. pallidum* generalization and localization of the parasite are constant phenomena, and according to the authors the infection is permanent, as the parasite can be recovered at any time by inoculation of material from superficial lymph glands of infected animals, even although the latter may have acquired a high degree of protection against the toxic effects. These facts have been utilized for the preservation of stock strains of *T. pallidum.* All that is necessary is to keep a sufficient number of infected animals to guard against the loss of the strain by their death. Serial transfers are unnecessary. When a strain has to be recovered for teaching or other purpose it suffices to excise a popliteal gland, emulsify it in saline, and make a testicular injection.

W. B.

Gärtner, W. Über die Häufigkeit der progressiven Paralyse bei kultivierten und unkultivierten Völkern. Eine statistische, biologische und Immunitätsuntersuchung über die Syphilis. [**On the incidence of general paralysis among civilized and uncivilized peoples. A statistical, biological, and immunological study of syphilis.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **92**, 341.

This is an elaborate statistical, biological, and immunological inquiry on the incidence of general paralysis of the insane in civilized and uncivilized peoples. The author deals especially with the dissemination of syphilis and paralysis according to age, sex, occupation, and locality, a great many interesting facts being related with reference to the diseases in foreign and especially uncivilized countries. The various theories which have been held to explain general paralysis are considered in some detail and are carefully analysed and criticized. It is impossible to give a short abstract of this paper, which runs to over 130 pages, but it should be consulted by those who are particularly interested as being an important contribution to the subject. W. B.

GRAM, H. C. *Studier over fibrinmængden i Menneskets blod og plasma samt nogle hermed forbundene problemer.* [B.] **[Studies on the fibrin content in human blood and plasma, together with problems connected therewith.]** København, 1921, 276 pp.

This is a thesis presented to the University of Copenhagen for a doctor's degree and embodies most of the author's original work, to which attention has already been directed on several occasions in *Medical Science.*

The study of the clotting of citrated plasma on recalcification has shown that the fibrin content of blood and plasma may be determined with considerable accuracy by recalcifying 2 c.cm. cell-free citrated plasma with 2 c.cm. 1 per cent. $CaCl_2$, $6H_2O$ and adding 9 c.cm. of a 0·9 per cent. sodium chloride. The recalcified plasma is kept at 35° C. for $1\frac{1}{2}$ hours in a glass beaker, and the clot is thrown out in several layers of filtering paper which absorbs the water, leaving a shining membrane. This fibrin membrane may be easily detached by throwing the paper into water. After washing with water, alcohol, and ether, the fibrin membrane is dried in the thermostat and weighed. The small amount of liquid left in the beaker serves as a control. It must not clot when a small amount of serum is added. It is shown that plasma in all cases met with contains sufficient prothrombin to precipitate all its fibrinogen under the conditions described above.

This technique gives as good or better results than older methods for determining the fibrin or fibrinogen percentage, though it is easier, more accurate, and may be carried out with smaller quantities of blood.

The fibrinogen percentage is shown to be a little higher than the corresponding fibrin percentage.

The mean error in the fibrin determination is found to be very small.

The citrated plasma required for the analysis may be obtained by centrifuging a mixture of 0·5 c.cm. 3 per cent. citrate and 4·5 c.cm. venous blood in a graduated tube—that is, in the same manner in which one determines the platelet count (by Oluf Thomsen's method) or the coagulation time. In order to avoid impurities of fibrinolysis the plasma used must be freed of leucocytes. A cell-free plasma in numerous experiments which included cases of fibrin deficiency showed no trace of fibrinolysis.

In order to calculate the fibrin percentage in pure plasma and pure blood one needs to know the partial volume of the blood-cells. As the 3 per cent citrate solution used is nearly isotonic, the cell-volume percentage may be determined either in the hematocrite or by centrifuging for $1\frac{1}{2}$ hours with an electrical separator at 3,000 revolutions a minute. The cell-volume percentage is calculated from the equation. Vol. per cent. = $100\ P/B$, where P is precipitate in citrated blood, and B the quantity of blood used. The formulae for calculating the fibrin percentage in plasma and blood are respectively:

$$F_p = (C_b - P)\ 100\ W_f / 2\ (C_b - P - C)$$

$$F_b = (C_b - P)\ 100\ W_f / 2\ (C_b - C)$$

where F_p is the per cent. fibrin in plasma, F_b the per cent. fibrin in blood, C_b the volume of citrated blood in c.cm., P the volume of cell precipitate, W_f the weight of fibrin in grammes in 2 c.cm. of citrated plasma, and C the volume of citrate (0·5 cubic cm.). The cell-volume per cent. in normal men lay between 51 and 43, in normal women between 45 and 37, the mean values being 48 and 41 respectively. Cases with a cell-volume smaller than 36 per cent. have been classified as anaemias, those larger than 55 per cent. as polycythaemias. The fibrin content of 100 c.cm. pure plasma in normal men is about 0·27 per cent., and 0·29 per cent. in women. Corresponding values for 100 c.cm. pure blood were found to be 0·14 per cent. and 0·17 per cent. The fibrin content does not show variations in the course of the day or in relation to meals.

In compensated heart diseases, afebrile cases of emphysema or asthma without bronchitis, stomach diseases (except cancer), non-infectious nervous diseases, and neuroses, the fibrin content varies within the normal limits. In afebrile simple anaemias and polycythaemia the fibrin percentage in plasma is about the normal mean value, while in pure blood it is increased in anaemia, decreased in polycythaemia. In leukaemia and pseudo-leukaemia (especially myeloid leukaemia) a slight increase in the fibrin percentage in plasma may be met with. In haemophilia increased fibrin percentages were nearly always found, though no infectious complications were present. In a case of scurvy with stomatitis the fibrin was increased, while it was normal in a case of genuine purpura.

A diminution of the fibrin percentage in plasma (i. e. less than 0·20 per cent.) was found in a few cases of pernicious anaemia, especially one that by the post-mortem showed a distinct fatty degeneration of the liver. The aplastic types of anaemia do not show especially low fibrin percentages. In 14 cases which by autopsy showed considerable destruction of the liver parenchyma (fatty degeneration, amyloid, atrophy, and cirrhosis) the fibrin percentage in plasma was lower than 0·20 per cent. in six, though many of these patients suffered from infectious diseases which tend to increase the amount of fibrin. These two groups—pernicious anaemia and liver degeneration—were the only ones in which cases of fibrin deficiency were found. These findings seem to support the theory of the origin of fibrinogen from the liver, or at least tend to show that the liver influences the production of this body.

No evidence has been found that haemorrhagic diathesis ever is caused by a fibrin deficiency, though this may be an assisting factor in cases which also show thrombopaenia.

An increased fibrin percentage in plasma is met with in numerous infectious diseases: croupous pneumonia, broncho-pneumonia, rheumatic fever, pleurisy, erysipelas, suppurative infections, gonorrhoeal infections, scarlet fever, angina, and bronchitis, while the increase is slighter or altogether missing in cases of measles, typhoid fever, influenza, tuberculosis, syphilis, and malaria. The degree of 'hyperinosis' depends upon the character and severity of the infection. When the fever, falls the fibrin percentage begins to drop, generally reaching normal values within some weeks after the defervescence.

If one of the last-named diseases is complicated by an infection belonging to the first group there occurs an immediate rise in fibrin percentage. The difference between the two groups of infectious diseases often, but not always, coincides with the old division into 'phlegmasia' (local inflammation) and 'pyrexia' (general infection). This, however, is considered a coincidence, the hyperinosis being more dependent upon the properties of the virus than upon the seat of the infection. Without an investigation of the pathological anatomy and physiology of the fibrinogen-producing organs it is not possible to say whether the absence of pronounced hyperinosis in certain infectious diseases is due to paralysis or a lack of irritation of these organs. The latter supposition for several reasons seems the most probable.

In the infectious diseases proper the fibrin percentage in plasma is frequently found increased in cases of uncompensated disease of the heart, nephritis, and malignant tumours.

The hyperinosis in uncompensated diseases of the heart may be explained by infection in lungs predisposed by stasis and oedema. The same cause may partly explain some of the high fibrin percentages found in nephritis, though there can be no doubt that the underlying infection of intoxication of the organism also plays an important rôle. In cancer the hyperinosis may be partly or wholly caused by infection of the ulcerated surfaces of the tumour, since in one case at least a 'closed' tumour did not show an increased fibrin percentage. However, the tumour itself may provoke an increased production of fibrinogen. A tumour obstructing the gall-ducts and causing intense icterus will nevertheless cause a distinct hyperinosis. A tumour giving rise to profuse metastases in the liver may—in spite of extensive ulceration of the primary neoplasm—still show a normal, and in one case even showed diminished fibrin percentage in the plasma.

By intramuscular injection of sterile milk one may provoke a distinct rise in the fibrin percentage. The explanation of this phenomenon may be sought in an irritation of the fibrinogen-producing organs by the foreign proteins which have not passed the alimentary canal. The same cause may explain the hyperinosis found in progressive chronic polyarthritis (infection?) and in the course of the normal pregnancy.

The intoxications with protein foreign to the blood are then ranged in line with those caused by proteins (?) of bacterial origin and by tumours. As to the hyperinosis constantly caused by pregnancy this tends to show that the liver is slightly irritated. No case of acute yellow atrophy of the liver in pregnancy, however, has been observed, while cases of eclampsia did not show any special variation, the 'locus minoris resistentiae' here being evidently the kidneys. The pathological substratum for the hyperinosis in infectious and toxic diseases may be sought in the slight hepatitis which generally accompany these. Only rarely is this hepatitis strong enough to cause a decay of the liver sufficiently violent to paralyse the fibrinogen production. A diminished fibrin content of the plasma is a 'signum mali ominis'.

The plasma colour has been determined by the method of Meulengracht. In normal men it was found to vary between 1 and 4, in normal women between 1 and 3. If the cause of the hyperinosis is a hepatitis, one must admit that there is no relation between the degree of hyperinosis and the degree of the bilirubinaemia. The study of the fibrin content in cases of severe liver degeneration, however, shows that even very extensive destruction of the liver parenchyma may not be accompanied by increased plasma colour, so that the fibrinogen production must be a different function of the liver.

It is also shown that even an excessive 'icterus per stasin' does not hamper the normal fibrinogen production or the infectious hyperinosis. The majority of these infections and intoxications, which cause hyperinosis, are also accompanied by a more or less pronounced leucocytosis. There are nevertheless several exceptions to this rule, as, for instance, chronic polyarthritis, and on the other hand the pronounced increase of the white cells in polycythaemia is not accompanied by hyperinosis, though the leukaemias will behave like infections with a slight tendency to fibrin increase. In a single case there was no reliable relation between the white cell count and the fibrin percentage. The latter may be increased even in cases with extreme leucopenia, while on the other hand one may find a pronounced deficiency of fibrin together with a marked leucocytosis. The great lability of the number of leucocytes, which is influenced by several factors, may somewhat obscure the relations. Also it must be remembered that though both leucocyte count and fibrin percentage increase rapidly at the onset of a toxic infectious process, the former will fall very quickly after the infection is overcome, while the fibrin percentage will take weeks to drop to the normal level. All things considered it seems as if hyperinosis and hyperleucocytosis are two independent effects of an intoxication which does not always influence both factors in the same way. Compared with the fluctuations of the leucocyte count, the fibrin level of the plasma seems to show a more sure, sensitive, and durable reaction against certain intoxications.

5 c.cm. citrated blood (0·5 c.cm. of 3 per cent. citrate + 4·5 c.cm. blood) from normal individuals which is kept at room temperature in a 5 c.cm. centrifuge tube will, after standing for 10 minutes, always show a layer of plasma narrower than 0·1 cm., i.e. traces of sedimentation. In order to make the difference between normal individuals, as for instance between the two sexes, clearly visible, a longer time of observation (1 hour) is needed. The velocity of sedimentation of the corpuscles depends upon the temperature, upon the percentage cell-volume, and upon the degree of auto-agglutination of the blood-cells. The latter phenomenon depends upon the content of fibrinogen (and possibly other serum proteins) in the plasma. The higher the surrounding temperature and the fibrin percentage in plasma is, and the lower the cell-volume, the more the velocity of sedimentation is increased. A sedimentation of 0·1 cm. or more in 10 minutes is only met with in cases of hyperinosis or anaemia, while on the other hand a polycythaemia or fibrin-deficiency may cause the sedimentation to be zero after 10 minutes.

Apart from the results of the examination of a large material of ‘natural’ citrated blood, these relations have been proved by an experimental observation of different mixtures of washed red cells, citrated cell-free plasma, citrated serum, citrated plasma deprived of fibrinogen by heating, physiological saline solution and solutions of pure dialysed fibrinogen.

A ‘crusta phlogistica’ (buffy coat), i.e. a colourless upper layer of coagulated plasma, is generally not met with in normal venous blood, when 1 c.cm. is left to clot at room temperature in a small test-tube with a diameter of 9–10 mm. A ‘buffy coat’ of varying extension is formed when the velocity of sedimentation (anaemia and hyperinosis) or coagulation-time is increased. The influence of the first factor ordinarily is prevalent. Circumstances connected with the taking and conservation of the blood (narrow needles or unclean glasses) may shorten the clotting-time. Lowering of the surrounding temperature increases the coagulation-time, but at the same time diminishes the velocity of sedimentation.

An extreme blood-platelet deficiency (pernicious anaemia, &c.) or certain changes in the plasma found in haemophilia may prolong the coagulation-time and thus cause the formation of a ‘crusta phlogistica’ without an increase in the velocity of sedimentation. W. A. M. S.

Ashby, Winifred (1). **Study of transfused blood. I. The periodicity in eliminative activity shown by the organism.** *J. Exper. M.*, 1921, **34**, 127.

Ashby, Winifred (2). **Study of transfused blood. II. Blood destruction in pernicious anaemia.** *J. Exper. M.*, 1921, **34**, 147.

The authoress attempted to study the length of life of normal blood corpuscles and the mechanism of their removal from the circulation by observing the elimination of the transfused blood which it was possible to make when such blood is of a group unlike that of the recipient. In the present research the elimination of transfused blood was studied in individuals in Groups I, II, and III, receiving transfusions of blood obtained from individuals of Group IV. After transfusion with Group IV blood the recipient's blood is diluted with citrated serum in a leucocyte haemocytometer pipette, the mixture being expelled into a Wassermann tube. The native corpuscles are agglutinated, leaving the transfused corpuscles free so that they can be counted in a haemocytometer. Charts and tables of many cases are given, from which the authoress argues that the length of time that transfused blood remains in the circulation varies greatly, and, further, that the elimination is not a continuous process but takes place in cyclic crises. This periodic blood-destroying activity occurs both in males and females, and in the latter is coincident with menstruation. The elimination of the transfused blood probably takes place as part of a period of blood-destroying and blood-producing activity of the body, although direct evidence to this effect is lacking.

The second paper is taken up with blood-destruction in 33 cases of pernicious anaemia in which Group IV transfusions were made, the object being to determine whether or not there has been any haemolytic toxin at work. For this purpose curves of elimination of Group IV transfusions in pernicious anaemia cases were compared with those obtained from patients without blood diseases. Full data are presented of the observations made and the authoress concludes therefrom that there is not sufficient evidence to indicate the existence of a haemolytic poison as has generally been supposed. Some evidence is presented to show that periods of active blood-destruction, which are seen as the exception in pernicious anaemia cases during a series of transfusions, are due to the activity of the blood-destroying organs of the body rather than to the intrinsic fragility of the red corpuscles in pernicious anaemia. W. B.

Onohara, K. The physico-chemical state of sugar in the blood. *Brit. J. Exper. Pathol.*, 1921, **2**, 194.

(1) As shown by Kozawa, glucose causes swelling of human red corpuscles. But practically the same haematocrite results were obtained with human red corpuscles treated with the serum of a diabetic patient, normal serum with the addition of isotonic glucose solution, or isotonic glucose-saline solution. (2) It may therefore be assumed that sugar in the circulating blood is present in the same physico-chemical character as in the solution of free glucose. In other words, it must be present in the circulating blood in the form of free sugar. P. F.

BIOCHEMISTRY

Hess, A. F., McCann, G. F., and **Pappenheim, A. M. Experimental rickets in rats. II. The failure of rats to develop rickets on a diet deficient in vitamine A.** *J. Biol. Chem.*, 1921, **47**, 396.

The authors claim that they have established that young rats fed upon a diet which is complete except for a lack of fat-soluble vitamin develop keratitis and die of inanition or some infection. Their skeletons, however, show no changes which can be regarded as rickety, although there are signs of a lack of active osteogenesis. From this the conclusion is drawn that a deficiency of the fat-soluble vitamin does not produce rickets. It must be remarked that in so far as the authors claim that deficiency of fat-soluble vitamin is not a contributory factor in the production of rickets, they are at variance with well-established work (Mellanby, McCollum, and Park).

R. A. P.

McCollum, E. V., Simmonds, N., Shipley, P. G., and **Park, E. A. Studies on experimental rickets. VIII. The production of rickets by diets low in phosphorus and fat-soluble A.** *J. Biol. Chem.*, 1921, **47**, 507.

In this further contribution, it is made more evident than before that rickets is due to a complex of factors. Emphasis is laid upon the conclusion that the production of a condition in the rat resembling very closely human rickets is produced by two sets of factors. On the one hand a specific disproportion between the amount of calcium and phosphorus in the diet, in which the phosphorus is relatively low and the calcium relatively high; on the other hand an insufficiency of the factor usually known as fat-soluble A. Deficiency in calcium and phosphorus produced a pathological condition in the skeleton quite distinct from rickets; and when in addition there was a deficiency of fat-soluble A, osteoporosis was developed, and not rickets. The work is supported by a detailed description of the types of lesions found. If further established it will go a long way to solve the conflict of evidence as to the causes of rickets. R. A. P.

Howland, J., and **Kramer, B. Ca and P in the serum in relation to rickets.** *Am. J. Dis. Child.*, 1921, **22**, 105.

The calcium content of the serum of children is slightly higher than that of adults, 10 to 11 mgm. per 100 c.cm. being the usual figure in childhood, whereas in adults the average content is 9 to 10·5 mgm. If cases with frank tetany are excluded, the serum of rachitic children shows a normal calcium content in about 50 per cent. of cases. In the remainder a slight reduction in calcium is present. The inorganic phosphorus content of the sera of children suffering from rickets is, however, very definitely lowered. In healthy children the inorganic phosphorus averages 5·4 mgm. per 100 c.cm., being slightly higher in breast-fed than in bottle-fed infants. In rachitic children, the content in inorganic phosphorus ranged from 0·6 to 3·2 mgm., the average being 2 mgm., or less than half the normal amount. In cases treated with cod-liver oil the amount of calcium present was unaffected, but a striking rise in the phosphate content coincided with clinical and radiographic evidence of improvement. The authors suggest that this deficiency in inorganic phosphorus leads to a diminution in the relatively insoluble tricalcic phosphate, with resulting inadequate precipitation of this salt. Their findings may be compared with the paper of McCollum, Simmonds, Shipley, and Park (*J. Biol. Chem.*, 1921, **47**, 507), who were able to produce rickets in animal experiments with a faulty ration deficient in P and fat-soluble A, but containing adequate calcium. O. L. V. de W.

Rosemann, R. Beiträge zur Physiologie der Verdauung. VIII. Die Bedeutung der Chlorverarmung des Körpers für die Magensaftsekretion. [**The effect of reduction of chlorides on the gastric juice.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 1.

The author has previously shown (*Arch. f. d. ges. Physiol.*, 1911, **142**, 208) that when the chloride content of the body has been reduced by 20 per cent. the HCl content and the total amount of gastric secretion is much reduced, and finally secretion stops and appetite vanishes. Quite different conditions were reached recently by Takata, who found the gastric secretion was much less affected. Among the causes for discrepancy is the inadequate nutrition of Takata's dog, which lost 22 per cent. of its weight; the autolysis of muscle substance would liberate enough chloride to enable gastric juice with nearly normal HCl content to be secreted. C. L. E.

Gorham, F. D. Variations of the acid concentration in different portions of the chyme, and its relation to clinical methods of gastric analyses. *Arch. Int. Med.*, 1921, **27**, 434.

In the 'fractional method of gastric analysis', it is assumed that the gastric chyme after a test meal is a homogeneous mixture, and that the small portion aspirated represents the acid concentration of the gastric contents as a whole. The author removed the fasting contents of the stomach, and gave a test meal consisting of 30 gm. dry shredded wheat biscuit and 400 c.cm. of water. Forty-five minutes later 10 c.cm. portions were aspirated in rapid succession until the stomach was completely emptied. Acidity was determined by the Toepfer method. In the majority of the patients examined the successive samples showed marked variations in acidity. He points out that there is considerable experimental evidence that the gastric chyme, even after a liquid meal, is not a homogeneous mixture, as far as acidity is concerned. The acidity as ascertained by the fractional method of removing samples would therefore be dependent on the position of the tip of the tube, a position which is constantly varying. For a quantitative analysis of gastric contents the stomach must be completely emptied. O. L. V. de W.

Meyer-Bisch, R. Untersuchungen über den Wasserhaushalt. II. Über den Einfluss kleinster Kochsalz- und Zuckermengen auf die Brustganglymphe des Hundes. [**Water metabolism. The influence of minimal quantities of sugar and sodium chloride on the thoracic lymph in the dog.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 381.

The author has shown that in certain stages of pulmonary tuberculosis the water metabolism is so deranged that a thickening of the blood takes place to a degree almost unknown in other conditions. By the injection of a single dose of tuberculin an increase in weight occurs due to the body taking up water, and the viscosity of the blood and its total solids decrease.

This also occurs to a certain extent when injections of small quantities of sugar or salt solutions are given. For example, the night-sweats disappear when only 2 c.cm. of a 10 per cent. sugar solution are injected. The same is the case with a 10 per cent. solution. The injections may be repeated with increasing benefit. The author has attempted to obtain an experimental explanation for this obscure effect by observing the lymph-flow from the thoracic duct with the change in its composition.

After the injection of salt solution, the albumin content of the lymph decreases after a short preliminary rise, with a general decrease in lymph-flow. Sugar solutions produce a similar effect: there is a retention of water and proteins in the tissues. Hence in the treatment of tuberculosis, tuberculin, which is a lymphagogue of the first order, may have its place taken in the effect it produces on the water metabolism by sodium chloride or sugar, which are lymphagogues of the second order. C. G. L. W.

Becher, E. Ueber den Einfluss grosser Aderlässe auf die bei nephrektomierten Hunden in Blut und Muskelgewebe angehäuften Retentionsprodukte. [**Effect of large bleedings on the retention of waste products in the blood and muscles of nephrectomized dogs.**] *Ztschr. f. klin. Med.*, 1920, **90**, 7.

A detoxicating action has been ascribed to bleeding in uraemia, the assumption being that the removal of accumulated waste products by blood-letting will have a favourable action on the patient. The author finds that in nephrectomized dogs the actual rise in non-protein nitrogen is almost as great in the muscles as in the blood. Since the muscles constitute 45 per cent. of the body-weight, while the blood only amounts to 8 per cent., the muscles must be regarded as the great storehouse of the nitrogenous waste products. On completely anuric dogs (bilateral nephrectomy) bleedings up to 45 per cent. of the total blood-volume—that is, very much larger bleedings than are ever attempted in man—produced no fall in the non-protein nitrogen of the blood and muscles. On the contrary, a definite rise usually followed, possibly due to the increase in protein katabolism, which was found by Bauer to follow blood-letting. O. L. V. de W.

Magnus Levy, A. Natriumbikarbonate und Kochsalzödeme. [**Sodium bicarbonate and sodium chloride oedema.**] *Ztschr. f. klin. Med.*, 1921, **90**, 287.

The production of oedema by sodium bicarbonate has long been recognized owing to the treatment of diabetics with large quantities of this salt. Apparently oedema can only be produced by sodium bicarbonate in cases in which sodium chloride is also productive of oedema, and not in healthy young people. The author has studied the action of equivalent amounts of the two salts in nephritics. Bicarbonate always increased the oedema, but to a less extent than the chloride. The oedema fluid after administration of bicarbonate contains 0·6 per cent. sodium chloride, the latter salt being derived from the food. In cases in which a bicarbonate oedema is produced on a diet poor in chlorides, the chloride of the oedema fluid is derived from the tissues. He gives figures to show that in severe cases of nephritis there is a definite excess of sodium chloride in the tissues (*rétention sèche*). O. L. V. de W.

Leiter, A. Observations on the relation of urea to uraemia. [**B.**] *Arch. Int. Med.*, 1921, **28**, 331.

A full review is given of the theories that have been advanced up to the present time in explanation of uraemia. The author has experimented on the effects of the intravenous injection of urea in dogs. A $33\frac{1}{3}$ per cent. solution of urea was employed, and was run in at the rate of 2 gm. per minute, until twitchings or convulsions interfered with the injection. An average of 1·1 per cent. of body-weight of urea produced toxic symptoms such as twitchings, generalized tremor, coma, and death. Salivation and vomiting were early and constant symptoms. Haematuria was of frequent occurrence. Necropsy findings showed haemorrhages in the mucosa of stomach and intestines, hypostatic oedema and congestion of the lungs, and fatty degeneration and cloudy swelling in the kidneys. The blood at death showed an average urea content of 1,383 mgm. per 100 c.cm. Carefully purified urea gave the same results as a commercial preparation. With one ureter ligatured, an average of 0·8 per cent. of body-weight sufficed to produce symptoms. O. L. V. de W.

Stephan, R., und **Wohl, E.** Untersuchungen über das proteolytische Serumferment. [**Proteolytic ferments in serum.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **24**, 391.

In the discussion of the so-called protective ferment theory on which Abderhalden has based his methods for the diagnosis of pregnancy, carcinoma, &c., Stephan has been a strong critic of the hypothesis. In the present paper the authors go further with their criticism. They point out that the idea that a serum is proteolytically inactive is incorrect. Each serum has a distinct proteolytic activity, but this is masked by the physico-chemical condition which prevents the action taking place *in vivo*. If the serum be shaken with chloroform, for example, the ferment becomes active. The authors believe that many of the antiferments will lose their place in the same way, as the effect which is thought to be dependent on them is due to a change of state of the serum. C. G. L. W.

Nonnenbruch. Über extrarenale Ödemgenese und Vorkommen von konzentriertem Blut bei hydropischen Nierenkranken. [**Extrarenal oedema, and concentrated blood in hydropic nephritis.**] *Deutsches Arch. f. klin. Med.*, 1921, **136**, 170.

The clinical investigations of oedema of recent years have tended to place more importance on extrarenal factors and to put the kidney in a position where it does not play an all-important part. This is partly due to investigation of war oedema, where little or no changes were found in the kidneys. On the other hand it is known that there are no changes in the kidneys which inevitably give rise to oedema. It is probable that peripheral vascular changes which exclude the kidney are of equal importance with any pathological condition of the organ.

A concentrated blood seems to be of rare occurrence in these conditions, and in war nephritis Thannhauser in a series of 800 cases never observed this condition.

Nonnenbruch has examined the blood count, refractometric number (albumin, &c.), sodium chloride, and rest nitrogen content in a number of cases with oedema. Here a concentration of the blood was made out. It would appear that in hydropic diffuse nephritis the blood may be concentrated, and that as a consequence it is not necessary to assume a hydraemic plethora. The oedema is of purely extrarenal origin; at the same time it is not asserted that the kidneys do not take part in the process.

In diuresis experiments with these cases, produced by giving 1,000 c.cm. of water or weak tea inside of 15–30 minutes, the hourly water elimination was followed during the ensuing four hours.

In normal cases practically all the water was eliminated during this period. The blood was if anything somewhat more concentrated (blood count); with kidney cases there was greater variation. If the water elimination be bad it points to a renal disturbance.

In the greater number of kidney cases with oedema the blood is either hydraemic or normal in concentration. In some cases one may find a more concentrated blood, pointing to an extrarenal origin of the oedema. This condition does not occur often, owing to opposing factors which tend to dilute the blood. The author lays great weight on blood counts, done after the hand has been immersed in hot water and massaged, as an indicator of the concentration. C. G. L. W.

Löwy, J., and **Mendl, R.** Über Schwankungen des Rest-N im menschlichen Blute unter dem Einflusse von Aderlassen und Glühlichtbädern. [**Variation in the rest nitrogen in human blood after venesection or light baths.**] *Deutsches Arch. f. klin. Med.*, 1921, **136**, 112.

The authors have examined the effect on the rest nitrogen in the blood, sodium chloride content and serum refraction (protein) after venesection and light baths. They find that both these measures lead to hydraemia.

A mobilization of the extractive nitrogen of the normal tissues, if it takes place at all, only does so to a small extent.

That it may take place in a condition such as acute articular rheumatism seems to be shown by one experiment. C. G. L. W.

Hahn, A. Der Doppelstickstoff, ein Diagnosticum für endogenen Eiweisszerfall, insbesondere für okkulte eitrige Prozesse. [**The 'Doppel' nitrogen, a diagnostic for endogenous protein destruction, especially for occult purulent processes.**] *Biochem. Ztschr.*, 1921, **121**, 262.

Certain conditions will alter the amount of the polypeptide and peptone material in the blood, the intermediate products of protein breakdown.

The estimation of the amount of these bodies can be obtained by determining the N in the serum minus protein, and subtracting from it the value for the N in the serum minus intermediate products. By the use of a method outlined the author has determined the amount of the intermediate products in the blood under several conditions. He terms this the 'D.N.' or Doppelstickstoff.

In normal sera, and in the sera of patients without parenteral proteid destruction, the D.N. value is about 10 or under, reckoned in his units. For cases such as pyelitis or tuberculous nephritis, in which a certain amount of protein breakdown would be expected, the D.N. value is increased, values up to 34 being given. Carcinoma in the ulcerating stage gives values higher than 10; in the proliferating stage values under 10 are obtained.

It is important to use the serum for these results because it has been found that whereas under pathological conditions the D.N. substances are found in the serum, in the normal state there are more relatively in the corpuscles.

The values can be compared with the R.N. (rest nitrogen).

R. A. P.

DOISY, E. A., and **EATON, E. P.** **The relation of the migration of ions between cells and plasma to the transport of carbon dioxide.** *J. Biol. Chem.*, 1921, **47**, 377.

By the use of new methods of analysis, the authors have confirmed the fact that sodium and potassium do not migrate through the wall of the blood-cell, and that the main change as CO_2 is passed into the blood is a migration of chlorides. They find an increase of corpuscle volume with increasing tension of carbon dioxide. R. A. P.

ATZLER, E., and **LEHMANN, G.** Über den Einfluss der Wasserstoffionenkonzentration auf die Gefässe. [**The influence of hydrogen-ion concentration on the blood-vessels.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 118.

By perfusion of frogs with gum-Ringer's solution of varying P_H, with an apparatus previously described, it was found that between P^H 5 and P_H 7 there was no change in the perfusion rate; below P_H 5 there was vasoconstriction irrespective of the nature of the anion, while above P_H 7·1 there was also vasoconstriction. Whether the central nervous system was intact or destroyed was immaterial. The authors incline to an explanation along the lines of the 'Quellung' hypothesis. C. L. E.

HANDOVSKY, H. Quantitative Beiträge zur Frage des Zusammenwirkens von Ionen und organischen Giften. [**Quantitative studies on the synergy of ions and organic poisons.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 173.

Saponin causes haemolysis of red cells less readily when these are suspended in isotonic sugar than when in isotonic NaCl solutions. In isotonic mixtures of the two substances the reduction of resistance to haemolysis is proportional to the NaCl concentration. The causes of this are discussed. C. L. E.

CUSHNY, O. R., and **LAMBIE, C. G.** **The action of diuretics.** *J. Physiol.*, 1921, **55**, 276.

A study of the action of certain diuretics on the blood-flow through the rabbit's kidney. For measuring the renal circulation a modification of the method of Barcroft and Brodie was employed. The method of action of caffeine, pituitary extract, strophanthin, sodium sulphate, urea, gum solution, and adrenalin were studied. In the case of one diuretic only —pituitrin—did the increase in urinary excretion appear to depend directly on the increased blood-flow through the kidney. With caffeine the diuresis begins before the accelerated flow, and continues after the flow has become normal again. In the case of salts and of urea, diuresis is not necessarily accompanied by an increased rate of renal circulation. No diuretic action of strophanthin could be demonstrated. O. L. V. de W.

Joël, E. Zur Visco- und Stalagmometrie des Harns. [**On the viscosimetry and stalagmometry of the urine.**] *Biochem. Ztschr.*, 1921, **119**, 93.

The paper includes a number of estimations of the two values for urine given in the title. The relative viscosity of normal urine as compared with distilled water was found to lie between 1·0 and 1·05. The presence of formed elements and of colloidal bodies in the urine raised the viscosity. But there was no characteristic viscosity value for disease. The same type of result was got for the determinations of surface tension. The presence of serum, or more notably of bile, was found to cause a considerable lowering of surface tension. An artificial mixture resembling urine and free from colloids had the same tension as distilled water; this was, however, lowered slightly by the presence of glucose or acetone, and of course more notably by bile and serum. As is to be expected, measurements of this sort are only a rough indication of the type of disease to look for; no help can be looked for in the differential diagnosis of cases where bile appears in the urine. R. A. P.

Murschhauser, Hans. Welche Zuckerart wird vom Säugling im Harne ausgeschieden, wenn die für ihn festgestellte Assimilationsgrenze für Rohrzucker in der Nahrung überschritten wird? [**What kind of sugar does the infant split off in its urine if it exceeds the tolerance limit for cane-sugar in its diet?**] *Biochem. Ztschr.*, 1921, **119**, 328.

The experiments show that if considerable amounts of cane sugar are fed to the infant the urine contains glucose, laevulose, and unchanged cane sugar. This shows that the ferments for inversion are not completely developed in the infant. A method is given for estimating the amounts of the various sugars in the urine. R. A. P.

Mertz, A. Blutzuckeruntersuchungen im Säuglings- und Kindesalter. [B.] [**Investigations on blood-sugar in infancy and childhood.**] *Archiv f. Kinderh.*, 1920, **68**, 254.

A review of methods of estimating blood-sugar with a summary of observations on the sugar content of the blood in childhood up to the date of publication, mainly from the German literature. O. L. V. de W.

Hermanns, L., und **Sachs, P.** Über das Wesen der Ehrlichschen Diazoreaktion. I. und II. Mitteilungen. [**The nature of the diazo-reaction cf Ehrlich. 1st and 2nd communications.**] *Ztschr. f. physiol. Chem.*, 1921, **114**, 78 and 88.

The substances in the urine which give Ehrlich's diazo-reaction may be extracted in two ways. The first consists in combining them with dichlorodiazobenzene chloride and extracting the dyes formed with a mixture of ether and pyridine. The second method is to concentrate the urine, acidify it, and shake out with ether. In this way a reducing substance is obtained which gives both the diazo and aldehyde reactions of Ehrlich. An azo dye was extracted from the urine of a patient suffering from carcinoma of the liver, and the substance in the urine responsible for the dye formation is considered by the authors to be 4-hydroxyindole-3-acetic acid, a possible degradation product of tryptophane. H. W. D.

Hoppe-Seyler, G. Über die Zusammensetzung der Leber, besonders ihren Eiweissgehalt in Krankheiten. [**The composition of the liver, with particular regard to its protein content in disease.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 67.

The total weight, dry substance, total protein, coagulable and non-coagulable nitrogen, fat content, and ash of livers taken from 43 cases *post mortem* are determined. The results are tabulated together with the microscopic findings. H. W. D.

Lesser, E. J. Die räumliche Trennung von Glycogen und Diastase in der Leberzelle. [**The spatial separation of glycogen and diastase in the liver cell.**] *Biochem. Ztschr.*, 1921, **119**, 108.

This is another contribution to the question as to how glycogen and its ferment diastase co-exist in the cell. When a frog's liver is perfused for four hours after death with oxygenated Ringer's solution there is a continuous loss of glycogen. This is used as a measure of the diastatic activity. If the perfusion is performed with a hypertonic solution, which dehydrates the liver tissue, the loss of glycogen in the four hours may be increased as much as four times. The reaction of the fluid makes a considerable difference. Perfusing with an isotonic saline solution, it was found that about twice as much glycogen was destroyed in the experimental period at a reaction of P_H 6·4 as compared with P_H 7·4. It was also found that the reaction of the fluid influenced the taking up of water by the liver-cells from the perfusing fluid. In a discussion of the matter, it is concluded that the dehydration of the cells acts so as to bring the diastase and the glycogen into contact, though it is left a little vague as to whether this is a question of alteration of cell colloid or some other condition.

It is interesting (a fact not noted by the author) that Langfeldt showed that the optimum P_H for the action of calf-liver diastase upon glycogen was 6·2. This would seem to make it probable that the real action of the hypertonic solution in dehydrating the liver-cell is to make the reaction of the cell more acid, and so increase the rate of reaction of the diastase.

R. A. P.

Gasser, H. S., and **Newcomer, H. S.** **Physiological action currents in the phrenic nerve. An application of the thermionic vacuum tube to nerve physiology.** *Am. J. Physiol.*, 1921, **57**, 1.

An apparatus is described based on the thermionic vacuum tube by which physiological action currents as they appear in the phrenic nerve may be recorded. The results are discussed. W. C.

McGuigan, H., and **Atkinson, H. V.** **The effect of haemorrhage on the sympathetic nerves.** *Am. J. Physiol.*, 1921, **57**, 95.

All nervous impulses that increase the sugar in the blood pass over the sympathetic system. Haemorrhage causes a hyperglycaemia, it also stimulates or sensitizes the sympathetics as judged by the response to injections of adrenalin. By the use of drugs that are known to stimulate or depress the centres it is shown that the greater influence of the haemorrhage on the vasomotor mechanism is peripheral. W. C.

Fulton, J. F., Jr. Studies on neuromuscular transmission. I. The action of novocaine on muscle nuclei. *Am. J. Physiol.*, 1921, **57**, 153.

This ingenious but highly speculative paper tries to demonstrate that the 'receptive substance' of the muscle is situated within the nuclei of the muscle-fibres. W. C.

Roca, J. On the relative amounts of depressor and broncho-constrictor substance obtainable from the anterior and posterior lobes of the fresh pituitary gland. *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 1.

Abel and Nagayama have shown that the addition of mercuric chloride to a concentrated pituitary extract precipitates the pressor and oxytocic hormone; the depressor substance remains in solution. The author has used the non-precipitable fraction to estimate the depressor substance. The glands were collected from slaughtered oxen, and the lobes separated at once. These extracts also contain broncho-constricting properties. Extracts from the posterior lobe are seven or eight times more depressant than similar extracts of the anterior lobe. The broncho-constricting action is also quoted.

Chloroform extracts from both lobes in a dried state a substance possessing a histamine action. The posterior lobe yields more. The author believes it to be histamine itself. C. G. L. W.

Dale, H. H., and **Dudley, H. W. On the pituitary active principles and histamine.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 27.

Abel and Nagayama believe that histamine is produced during the hydrolysis of the pituitary principles. This is denied by Dale and Dudley. who have subjected pituitary extract to hydrolysis and report the results of blood-pressure experiments and tests on the uterus of the guinea-pig. They compared the oxytocic and depressant action of the hydrolysate and of histamine itself. These do not correspond. Histamine, if present at all, occurs in such minute amounts that its chemical identification is impracticable. C. G. L. W.

Führer, H. Die Wirkungsstärke der Narkotica. [**The effective strength of narcotics.**] *Biochem. Ztschr.*, 1921, **120**, 143.

Traube, J., und **Klein, P.** Experimentelle Beiträge zur Theorie der Narkose. [**Experimental contribution to the theory of narcosis.**] *Biochem. Ztschr.*, 1921, **120**, 111.

These two papers are conveniently taken together. Traube originally suggested that narcotics such as alcohol were, in general, substances which lowered the surface tension of water. Such substances will, by the Gibbs principle, be absorbed on an interface, and will therefore pass more readily into the cell. As to their action when in the cell, he does not seem to have made more than the claim that substances of this class have been shown to influence the swelling of colloids, oxidation changes, and generally to interfere with the action of the cell. The theory involves the proof that substances which have a narcotic action have a low surface tension in narcotic concentrations. This was often the case, but there were notable exceptions (such as benzol) in which aqueous solutions showing narcotic and haemolytic properties were found to have the same surface tension as water. This difficulty has been considered by Traube in the above communication. The exceptional substances are those of low solubility in water. It appears that these aqueous solutions have present in them colloidal droplets. These, under the ultramicroscope, show the Tyndall phenomenon. Solutions in which droplets of this nature are present show the same surface tension in the stalagmometer as water. In this way, it is considered that some of the main difficulties are cleared up.

Fühner directs his research to the more practical aspect of the narcotic theories, how far they can be relied upon to give an accurate idea as to the narcotic strength of a given substance. He has compared the narcotic strengths of a large number of substances upon the frog's heart, finding that in many cases, notably benzol and the halogen-containing narcotics, Traube's views do not hold. On the whole, it is better to fall back upon the Meyer-Overton view of the partition between oil and water. In some cases the effect can be predicted from the solubility in water or in salt solutions of a given body.

In criticism of the above, some of the discrepancies found by Fühner are just the ones which Traube claims to have cleared up in the paper above. It is to be confessed, however, that they do not help matters as a practical test. If this type of view is not pressed too much, it is very helpful as a guide. After all, both the surface tension and the power of dissolving in fat must influence the entry of a substance into a cell, and probably influence, too, its behaviour inside the cell. But it seems irrational to put out of court more especially chemical types of action which must play their part in so complicated a system as the living cell. R. A. P.

Ohlsson, E. Die Abhängigkeit der Wirkung der Succinodehydrogenase von der Wasserstoffionenkonzentration. [**On the effect of the hydrogen-ion concentration on the action of the succino-dehydrogenase.**] *Skandin. Arch. f. Physiol.*, 1921, **41**, 77.

Thunberg has demonstrated the existence of ferments which remove hydrogen from certain dibasic aliphatic acids—the 'donator' substances—and transport the hydrogen to oxygen or to other reducible substances such as methylene blue—the 'acceptor' substances. These ferments are called 'dehydrogenases'. They are specific for each special donator substance. The present paper deals with the ferment 'succino-dehydrogenase', which reduces succinic acid to fumaric acid. The preparation of this enzyme is described in detail and the effect of temperature and hydrogen-ion concentration on the reaction has been studied in detail. W. C.

Brown, J. H. Hydrogen ions, titration, and the buffer index of bacteriological media. *Proc. Soc. Exp. Biol. & Med.*, 1921, **18**, 285.

Titration of bacteriological media reveals the buffer qualities of a medium which are not shown by a hydrogen-ion determination. The titration of different samples of bouillon of supposedly the same composition showed great variations in buffer content.

If the limiting hydrogen-ion concentration is sought for quickly a poorly buffered medium should be used. If a large amount of growth is desired the medium should contain a high concentration of buffers.

In a bouillon of low buffer index a small amount of glucose may be sufficient to produce a high terminal acidity, whereas the same organism may ferment a much larger quantity of the sugar in a medium with high buffer content and yet produce a terminal alkalinity. C. G. L. W.

Beumer, H. Zur Frage antigener Fettwirkungen. [**Antigen action of fats.**] *Biochem. Ztschr.*, 1921, **120**, 127.

Various types of bacterial fats and the ether extract of yeast were injected into young and adult guinea-pigs. There was no effect on the weight of the animals and no agglutination phenomena. [The author has neglected to take into account the dispersion state of the fatty compounds administered.—Abstr.] C. G. L. W.

Wolf, C. G. L. The survival of motility in mammalian spermatozoa. *J. Physiol.*, 1921, **55**, 246.

Rabbits' spermatozoa survived for at least nine days in a Tyrode solution which was buffered and to which glucose was added, the preparation being kept at a temperature approximating 0°. O. L. V. de W.

Embden, G., und **Laquer, F.** Über die Chemie des Lactacidogens. [**The chemistry of lactacidogen.**] *Ztschr. f. physiol. Chem.*, 1921, **113**, 1.

In 1914 Embden expressed the view, based on experimental work, that the lactic acid in muscle is derived from a hexose-phosphoric acid complex, which he called 'lactacidogen'. Full details are now given for the isolation from muscle of an osazone, which is identical with that previously obtained by Lebedev and by Young from yeast-hexose-diphosphoric acid. The authors do not claim to have established the identity of 'lactacidogen' with yeast-hexose-diphosphoric acid, but they regard the osazone as a definite derivative of 'lactacidogen'. In a long series of about a dozen papers in this volume (113) of the *Ztschr. f. physiol. Chem.* Embden and his collaborators bring forward much evidence in favour of the contention that where muscular activity is greatest there is most 'lactacidogen'. Thus, in cold-blooded animals (frog) there is more at 30° C. than at 0° C., and the mechanism of the change is not nervous since it occurs in muscles with the nerve-supply cut. On raising the temperature, 'lactacidogen' increases and the residual phosphorus decreases. On cooling summer frogs the reverse changes occur. The seasonal changes are correlated with muscular activity. The white muscles of rabbits contain about twice as much 'lactacidogen' as the less active red muscles. The breast muscles of the pigeon have a greater reserve of residual phosphorus than those of the fowl. Muscular work and strychnine convulsions decrease the amount of 'lactacidogen' in the white muscles of the rabbit. Phosphorus poisoning, associated with great muscular weakness, and Nagana fever have a similar effect. H. W. D.

Sollmann, T. Studies of chronic intoxications on albino rats. V. Arsenic trioxide. *J. Exper. Pharmacol. & Therap.*, 1921, **18**, 43.

Extremely small quantities of arsenic check growth. The amount given was comparable to that consumed in the Manchester arsenic epidemic. The need of careful watching of the patient when routine arsenic is administered is emphasized. The author inquires whether the supposed gain in weight when arsenic is given may not be due to a nephritic oedema. The results are in sharp contrast with the harmlessness of the drug to arsenic eaters. Tolerance appears to be acquired under special conditions which are not yet understood. C. G. L. W.

Zondek, S. G. Kalium und Radioaktivität. [**Potassium and radio-activity.**] *Biochem. Ztschr.*, 1921, **120**, 76.

The assertion of Zwaardemaker that the potassium in the body fluids functions by reason of radio-active qualities is subjected to an experimental analysis by the author, who reaches conclusions absolutely contrary to those of the Dutch physiologist. He shows that the radio-active qualities possessed by potassium are only 1/1,000,000,000 that of radium, and yet such amounts of emanation as 15,000 Mach units have no effect on heart action. Zondek is inclined to believe that the effect observed by Zwaardemaker in the recovery of the heart in diastolic cessation would have been observed without any operative procedures. C. G. L. W.

RADIOLOGY

Radiotechnique

Thedering. Neuere radiologische Erfahrungen. [**Some new radiological methods.**] *Strahlentherapie*, 1921, **12**, 796.

In this paper, besides other points, the author considers the course to be followed by the radiologist in cases of cancer of the eyelid, and in particular how far the eye can be irradiated without injury to vision. After combating the view usually adopted, that treatment should be centrifugal in respect of the glands, and asserting that it should be centripetal, he maintains that the dose of rays sufficient to cure a cancer of the eyelid, which has not actually invaded the eyeball, is usually not injurious to conjunctiva or cornea, provided that sufficient filtration (4 mm. aluminium) be used. The following is his method. ‘Apparatus: Apex, Reiniger, Gebbert and Schall. Müller boiling-tube. Hardness 9–10 Bauer = 25 cm. spark-gap. Current 2 m.a. On the first day the corresponding right or left inframaxillary glands from the angle of the jaw to the midline are irradiated for 15 minutes with 3 mm. filter. Distance: Filter—glands—eye 20 cm. If possible on the following day the eye itself is treated. The whole eye is left free by a circular aperture in a 2 mm. lead shield that protects the rest of the face. The whole exposed eye is now irradiated under the tube conditions given above for 12–15 minutes with 4 mm. aluminium filter. Eight to ten days later the same procedure over glands and eye is repeated, but this time for 10 minutes each and with 4 mm. filter. It is of the utmost importance in irradiation of the glands to define their position clearly and protect the field of irradiation carefully in order that distant foci of cancer cells may not be stimulated into growth by weak scattered radiation.’

W. S. L-B.

Radiodiagnosis

Costa et **Garcin.** Lésions du rhumatisme blennorrhagique constatées par la radiographie. [**Lesions in gonococcal rheumatism established by radiography.**] *J. de radiol. et d'électrol.*, 1921, **5**, 49.

The articular lesions produced by the gonococcus are very variable. The authors attempt to standardize the radiographic aspect obtained from the examination of over 200 cases.

(1) **Osseous lesions.** They are characterized by decalcification, osteoporosity, which may be acute (shading off of the osseous edges, flaky grey appearance of the image) or subacute ('pearly' appearance of the bone through the presence of vacuoles, and very rarely a veiled image). Bony ankylosis may follow, fusion of the opposing bony surfaces occurring on recalcification; as the cartilages have disappeared this fusion takes place rapidly. In the wrist the metacarpo-phalangeal joint of the thumb and the pisi-pyramidal joint always remain unaffected.

(2) **Periosteal lesions.** There are sometimes exostoses which are always limited and close together (the site of election is on the plantar tuberosities of the calcaneus), sometimes periostoses (fine bony needles parallel to the edges of the bone or as a collar round the epiphysis), sometimes a hyperostosis (very rare, since osteomyelitis is exceptional in blennorrhagia).

The integrity of the appearances by radiography does not eliminate the diagnosis of inflammation, but may only show that the lesions are limited to the synovial membrane for the time being. The evolution of the lesions shows that the infection passes across the surfaces rather than penetrates them; this explains why bony ankylosis is less frequent than fibrous ankylosis. Whereas in syphilis there is bone-formation and in tuberculosis bone-necrosis, in gonococcal lesions there is osteoporosity.

P. L.-B.

Dufour, H. Décalcification par trouble de la nutrition (neurasthénie) démontrée par la radiographie. [**Decalcification through disorders of nutrition (neurasthenia) demonstrated by radiography.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, Nov. 1920. (*J. de radiol. et d'électrol.*, 1921, **5**, 225.)

In the case of living persons, radiography is the best process for determining the condition of the osseous reserve in calcareous salts, but comparison is necessary. The author finds a healthy subject with a hand of the same length and thickness as that of the patient and radiographs the two hands on the same plate, at the same time, thus making comparison easy.

S. U. L.-B.

Engelmann, G. Über den Vorfussschmerz. [**On affections of the fore-part of the foot.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 311.

Sufficient attention is not paid to complaints of persistent and severe pains of the feet, particularly where they affect the metatarsal region, probably because the feet in this case show other changes, such as flat foot or pes valgus, which are attributed merely to changes in the instep, without taking into account the special affection which is the cause.

As a rule swellings and disease of the feet occur in adults, younger and older persons, men and women, and mostly in those doing much walking or standing.

For the purpose of studying these cases under Röntgen-ray examination plantar pictures of the forefoot were as a rule made, states the writer, the patient's foot resting lightly on the plate, not in any degree pressing or standing on it, and he shows in his photographs how the feet of the patients differ in the uneven arch and thickening of the metatarsal bones.

In his observations there is in all cases of pes valgus and planus, splay foot, &c., a distinct change in the metatarso-phalangeal joints; most frequently this occurs in both feet, but sometimes only in one.

Dividing his Röntgen findings into groups, illustrated by photographs, the author enters with considerable detail into the changes of malformation caused by these foot diseases, such as thinning or thickening of the fibrous tissue, occasional loop-like outgrowths, not infrequently subluxation of the first phalanx, and in all cases a bony edge on the metatarsus stretching in some acute cases from the dorsal to the medial side of the bone.

Thickening of the first metatarsal bones is found in almost all cases and develops sometimes into increased porosity at the head of the bone. All these troubles may be found as the result of chronic arthritis, diabetes, rheumatism, and syphilis.

He points out that X-ray findings often show decided affection of other than the painful toes, or where trouble has only been indicated in one foot the rays may show more marked trouble in the other foot. The patient may state that there has only quite recently been any pain, following a strain or blow, so that one expects to find a fracture of the painful bone, whereas the bony structure shows under X-rays distinct distortion caused by trouble of longer standing, to which the patient obviously paid no attention.

The writer emphasizes the importance of noting that where the neighbouring parts of the metatarso-phalangeal joint show greater or less changes (1) the tendon-sheaths, bursae, muscles, and nerves also show marked indication of change; (2) the proximal parts in the foot may be seriously affected, and (3) when the changes in the ankle show rapid progress of the disease further changes and continuance of the trouble should be speedily averted.

Indications for treatment in the various types of case are given in the paper.

F. E. R.

Thurstan Holland, C. On rarer ossifications seen during X-ray examinations. [B.] *Arch. Radiol. & Electroth.*, 1921, **26**, 105.

A careful paper with good illustrations that deals with unusual forms of ossification in foot and knee. The subject is important in respect of radiological diagnosis of fracture. In the foot some ten or eleven accessory bones are described, but the frequency of their occurrence varies. The most common in the author's experience is os tibiale externum, which is situated on the posterior and external side of the scaphoid. It is a definitely skeletal bone and is usually seen in adults, but has been found in a child of three years. In the case of sesamoid bones Holland says that the inner of the two found beneath the distal end of the first metatarsal in the tendons of the flexor hallucis brevis may be present in two, three, or, rarely, four pieces. The outer sesamoid is but rarely so affected. After referring to the os trigonum some space is devoted to the so-called os Vesalianum, and the author gives his reasons for considering the bone as epiphyseal; it is 'in reality an epiphysis at the base of the fifth metatarsal which usually joins on or before adult life, but in one form may remain separate in the adult'. He believes that Vesalius actually described the sesamoid of the peroneus longus. Reference is made to 'Kohler's disease' and it is pointed out that, whatever the pathology, this condition is associated with defective ossification of the scaphoid, a denser bone shadow being found in the affected foot. Comparison of the radiographs of the two feet or knees is fundamental when accessory bones are suspected, or the existence of a fracture is in doubt, for in the former instance the condition is almost certain to be bilateral. W. S. L.-B.

Radiotherapy

Webster, J. H. D. **X-ray treatment of two cases of otosclerosis.** [B.] *Arch. Radiol. & Electroth.*, 1921, **26**, 69.

The author states that as the early signs are usually unnoticed by the patients, advice is not sought until hearing has been markedly affected. The various theories as to the origin of the condition are then discussed somewhat at length, followed by a discussion on the earliest changes found and the reasons for believing that in its early stages the condition should be amenable to radiation treatment. A short account of the treatment of the condition since 1908 is given and the author then goes on to describe his own two cases; the first gave a 10 years' history and showed no improvement after treatment; the second gave a history of 8 years for right ear, 7 months for left ear, and after three months' treatment had improved distinctly. Treatment was continued and the improvement maintained. P. L.-B.

Morrell, R. A. **Some effects of radiotherapy upon fibrous tissue.** *Arch. Radiol. & Electroth.*, 1921, **26**, 78.

The scar tissue resulted from operative measures rather than from wounds in all the successful cases, that is, it was young tissue; in two unsuccessful cases the tissue was old. From the cases treated the author considers that radiotherapy might be much more widely used to remove young fibrous tissue which is likely to give rise to adhesions, pain, or limitation of function. Notes of several cases are given, and the article is concluded by a note on the general technique employed. P. L.-B.

Fränkel, M. Die Bedeutung der Röntgen-Reizstrahlen in der Medizin mit besonderer Einwirkung auf das endokrine System und seiner Beeinflussung des Karzinoms. [**The value of Röntgen rays in medicine, with their special action on the endocrine system and their influence on carcinoma.**] *Strahlentherapie*, 1921, **12**, 850.

The author opens this paper by a general discussion on the functions of the endocrine glands. He states the cause of the comparative immunity of the spleen to attack by tumour metastases as due to the power of the spleen almost invariably to destroy embryonic tissues transplanted into it, whereas in other organs these tissues not only increase in growth, but not infrequently lead to the formation of teratomatous tumours. He likewise points out that tuberculous affections seldom attack the spleen, thus proving the important part this organ plays in immunity reactions, and claims that X-rays increase its activity in this respect; the greater the effort of resistance in the diseased body the more far-reaching the effects of the Röntgen rays.

He quotes Aschner as showing that after extirpation of the spleen the functions of the thymus are increased; also Pasch, who shows in his critical work the connexion between the thymus and the bony system, as proved by the fact that after excision of the thymus defective growth and development of the long bones has been known to set in, and, on the other hand, delay in the healing of artificially-set fractures. Hence he deduces that lack of development in early life, while the thymus is in process of growth, is due to some disturbance of this organ. He quotes this in proof of a previous statement by him elsewhere, that the origin of rickets is probably to be found in such disturbances. When dogs have been thymectomized before reaching puberty the suprarenals become hypertrophied, the pituitary atrophies, and the thyroid gland is enlarged; inversely, castrated animals developed an enlarged thymus. The injection of thymus extract was followed by lowering of the blood-pressure and leucocytosis. Fränkel states that Schwarz and Lederer found that the substances in the thymus reducing blood-pressure are identical with choline, the antagonist of adrenalin, and that he, Fränkel himself, has already stated elsewhere that choline impedes the action of X-rays. He points out the extraordinary sensitiveness of the thymus gland to the effects of general nourishment and that the connexion between the thymus and bone rarefaction is clear. He maintains that it is quite wrong to suppose that this organ, which grows until puberty has been attained and then probably has reached its height, loses its power of function in later years. Microscopic observations prove that it continues to function in later years despite loss of weight. Not until the ages of forty to fifty, the age of increase of carcinoma tendencies, would there seem to be any eclipse of its powers accompanied by sclerosis of the parenchyma.

He quotes the experiments of Klose, Lampe, Liesegang, Hammar, and Hermann, of Breslau, to show the antagonism of the thymus to the ovaries, as proved when, by removal of the ovaries in a bitch, there followed a typical increase of lymphocytes, whereas after the removal of an enlarged thymus in a child a diminution followed; also the injection of thymus extract caused enlargement of the lymph glands; from which he deduces that the secretions of the thymus and ovaries are antagonistic in their effect on blood formation.

The author discusses the general effects of exposure of tumours to X-rays; under this treatment the cells become enlarged, the nucleus being chiefly affected, and an increase of nuclei has been observed. The chromatin is destroyed and in many cases absorbed into the cell protoplasm; vacuoles are produced in this protoplasm, which can be so large that the whole cell soon presents only a network of all that remains of its original structure. The altered tumour-cells are absorbed by the white blood corpuscles in the supporting tissue. The connective tissue itself becomes rich in fibrous strands and presents the appearance of a network; it sends its processes between the tumour-cells, collects these in ever-diminishing islands, and finally entirely displaces them. Fränkel quotes these as observations of

Simon. He states that according to Strauss the tumour-cells under the influence of X-rays show a complete change in their properties and may indeed be said to be neutralized. It has even been asserted that sarcoma-cells have, under the influence of the rays, changed into normal body-cells. On this assumption the healing of sarcoma by irradiation would be due not merely to destruction of the growth cells but rather to a cell metamorphosis. Should, proceeds Fränkel, this supposed cell metamorphosis prove an indubitable fact, then the extraordinary beneficial effects of irradiation on sarcoma would be explained without further question. There are, however, one or two effects to be noticed as against the glowing results of sarcoma treatment, and even in sarcoma a differentiation of sensibility to radio-treatment has been observed.

All reflections upon the use of excessively high or intense irradiation appear in a different light when we premise that we can do injury by means of the rays and may even create carcinoma, especially when an endocrine organ, which has a tendency to carcinoma, shows peculiar sensitiveness to rays and so can be injured by too strong doses.

Fränkel quotes Ribbert as stating that through the well-known results of actinotherapeutic measures on lymphocytes the influence of these cells on the curing of cancer has been established. According to his observation a spontaneous decrease of cancer epithelium has been definitely proved as caused by the influence of the lymphocytes. It is possible for a mass of round cells to be formed around carcinoma and lymphocytes, which are inimical to cancer. Ribbert's experiments, says Hans Meyer, would seem to show that this form of chemotherapy would prove to be of benefit if used in connexion with ray therapy, as the rays are well known to cause a decrease of lymphocytes, thereby releasing the beneficial toxin.

As to how far the blood itself comes in question in the destruction of carcinoma-cells is one of the oldest questions in the study of cancer. The search after the unknown body which protects those free from carcinoma and is lacking in cancer patients is never ceasing. According to the researches of von Kaminer there is present in normal serum a substance which destroys carcinoma and is lacking in cancer serum. The serum of nurslings posesses it in infinitely greater quantity than that of adults; even up to the age of 14 years this substance is very strongly developed, but diminishes notably in later years.

Continuing his conclusions on the power of irradiation in medicine, he points out its influence in the treatment of goitre and uterine haemorrhage, and the danger in these latter cases of over-exposure. He further refers to his work between 1911 and 1914 on the sterilization of criminals and mentally defectives, of women suffering from heart and kidney trouble, tuberculosis, and syphilis, through the use of X-rays, and adds that, as shown by him in his statements on strong doses, there was a quicker development of amenorrhoea and a higher tendency to nerve trouble, even to melancholia and psychoses, because of injury to the internal secretory function of the ovaries, whereas with smaller doses very beneficial results were shown, in the renewed vigour, youthfulness, and happier outlook on life of the patient.

Fränkel claims beneficial effects of irradiation in epilepsy, in Graves's disease, and in the increase of milk-supply in mammals. For diabetes he quotes the experiments of Beumer as shown in his article on Röntgen ray treatment of the suprarenals in diabetes, in a case of 6½ years' duration; the first treatment showed a diminution of sugar secretion of from 0·270 mg. to

0·153 mg. and after ten days of radiotherapy to 0·122 mg. He claims the amelioration of pain in arthritis and allied diseases by ray treatment.

One other point is to be noted in the specific influence of the thyroid gland on carcinoma, viz. in the constitution of malignant growths of the thyroid gland. These are sensitive to irradiation in such a high degree that one cannot judge of its effects fully by the surface swelling, but rather by the character of the tumour-cells. The struma maligna shows very varying histological characters; there are various kinds of carcinoma and different forms of sarcoma and sarco-carcinoma. If there be a difference in the action of the rays on each of such forms, this can only be proved by further experience. Out of six cases which Sudeck, says Fränkel, has treated, one case of sarco-carcinoma was entirely cured, and three cases of carcinoma of alveolar character were locally healed. On the other hand, malignant goitre shows as a rule very unsatisfactory clinical results. Only very seldom do these cases come for operation before the outer capsule of the thyroid gland is broken through and the outer parts infected. Sudeck has not yet succeeded in carrying out operations for removal of tumours of this kind with hopeful results.

The author quotes largely from the literature, but only gives references to his own papers. F. E. R.

Radium Therapy.

Regaud, Cl., Jolly, J., Lacassagne, A., Roux-Berger, J. L., Cesbron, H., Coutard, H., Monod, O., et **Richard, G.** Sur le traitement des cancers des lèvres par les rayons X et le radium. [**The treatment of cancer of the lip by X-rays and radium.**] *Bull. de l'Ass. franç. p. l'étude du cancer,* 1921, **10**, 321.

This is a paper emanating from the therapeutic department of the Radium Institute of Paris, and gives the experience there obtained during nearly two years in cancer of the lip. Twenty-two cases were treated, and it is important to note that a succinct account of each case is given with a report by the authorities as to the reasons for failure in all cases that did badly. A summary of the cases is as follows: one case was useless from a scientific point of view; in two cases there were large cervical glandular masses which developed subsequent to removal and cure of the primary growth (probably belonging to the group of epidermoid cancers); in two cases of epidermoid cancer the primary growth was treated with a defective technique, and the failure may be attributed to this cause; in one case an epidermoid epithelioma was refractory to the radiations by reason of an antecedent defective treatment with X-rays; finally there were sixteen cases in which either the primary growth was treated by a technique that the authors at the present time consider to be correct, or treatment has been efficacious from a curative point of view. The length of time clapsing since the so-called cure is, in some cases, only six months, but in a few it amounts to a year or more, and under any circumstances the results appear to be more hopeful than is customary when dealing with squamous carcinoma. Certain general rules are laid down. These are (1) the entire region of invasion by the new growth must be treated, preferably at a single time, otherwise in sections irradiated at short intervals; (2) the field of irradiation in which the entire new growth is included must be homogeneous; (3) for curative efficacy the first treatment must be reckoned on above all, i.e. a single treatment should be given, and this single treatment should cover a period of eight days whether X-rays or radium be used; (4) the new growth must receive the maximum dose of irradiation compatible with security of the normal tissues. The authors believe that in general better results are obtained with radium than with X-rays in cancer of the lip, and the majority of their cases have been treated with the former agent. Their method consists essentially in using small tubes (3–6 millicuries of emanation initially, or 2–3·33 mgm. radium element) disposed either superficially or by radium puncture, and tubes up to 40 in number of this intensity may be applied superficially or thrust into the substance of the tissue. They are left *in situ* for periods varying from eight to twelve days. Superficial application by cross-fire from the cutaneous and mucous surfaces is recommended when the thickness of the new growth is 20 mm. or less; when greater than this, use of radium puncture (the needles being introduced parallel) is better. For superficial use they place one element (1 mm. platinum enclosed in aluminium foil) at 1 cm. distance for each square centimetre of the new growth. A layer of gutta-percha 5 mm. thick separates the tubes from the tissues. In radium puncture, with a filtration of 0·4 mm. platinum and one needle for each 2–3 c.cm. of tissue to be irradiated, they reckon that they give $\frac{1}{3}$–$\frac{1}{2}$ millicurie per c.cm. of tissue treated in eight days. A small epithelioma will require 8–15 needles. So far as glands are concerned their degree of success has not been so great, and they say that for the time being surgical treatment should be preferred whenever possible. A short account is given of earlier publications on X-ray and radium treatment of cancer of the lip. Amongst their conclusions are: (1) subject to reserves cancer of the lip is curable by X-rays or radium even when extensive; (2) radium treatment is in all respects the method to be preferred over X-ray treatment; (3) a good technique is indispensable; (4) in the absence of a method that can be demonstrated as suitable for treatment of glandular metastases these ought to be removed surgically.

W. S. L.-B.

Radiobiology

Rohdenburg, G, L., and **Prime, F.** **The effect of combined heat and radiation upon transplanted animal tumours.** *J. Cancer Res.*, 1921, **6**, 101.

In the experiments described, mice and rat tumour in small fragments were exposed to varying degrees of heat and then inoculated into animals. Exposures to 40° C.–46° C. inclusive for times varying from 15 to 195 minutes. The lethal effect of heat was first seen with 40° C. for 195 minutes. As it had been shown that radiated albumins coagulate at lower temperature than non-radiated albumins, it was thought that this might apply to the killing of the cancer cell. Fragments of tumour were exposed to X-rays for 10–30 minutes—30 minutes = 3 erythema doses. Directly after radiation they were exposed to heat as above and then inoculated into animals. It was found that the combination of heat and radiation was lethal where the same degree of heat or radiation alone was not lethal. Whether heat or radiation be applied first appears to be immaterial.

In the discussion Greenough said that he thought there was no doubt that the experiments opened up a field for clinical application in the treatment of cases: Wood said that it was possible to obtain the absolute destruction of cancer-cells with either X-rays or radium, but that most internal tumours required so much radiation that serious, if not fatal, damage would be done to normal tissues. The maximum practical dose that a patient can stand has yet to be determined, but he thought that there is justification in giving radiation close to the limit. He thought it might be possible to apply heat by thermo-electrical means after giving the maximum dose of X-ray that the skin of the patient can stand, and in this way kill all the cancer-cells. Duane pointed out that seven years ago heat and X-rays were used in combination, but were applied together, and he thought that this must produce a greater effect.

Rohdenburg said that in the experiments lower degrees of heat were used over a much longer period than in the experiments previously reported, and the temperature was such as to be readily withstood by any normal tissue. P. L.-B.

Bagg, H. J. Interstitial injections of an active deposit of radium emanation in a rat carcinoma. *J. Cancer Res.*, 1921, **6**, 104.

An endeavour was made to use an active deposit of radium emanation as a local agent to control the growth of an experimental rat tumour. Interstitial injections of a radio-active salt solution of radium emanation retarded materially the growth of the tumours, and sometimes caused their regression. Histological changes were noted. Comparatively large doses could be injected without the escape of the radio-active solution into the surrounding tissues.

In the discussion Duane said it was important to emphasize the great danger of this method as the alpha-rays are used. Stone thought that the alpha-rays might be used in the infiltration method ; he contrasted the use of radium with the use of the cautery, and thought that in using the method the very smallest doses must be employed, so as to get the biological effect and not a local caustic effect on the tumour itself. Coley said that at the Memorial Hospital the method has been employed considerably, but that none of the results had led to the belief that it was likely to be of permanent use therapeutically ; the cases which benefited were those in which the tumour was localized by the surrounding tissues.

In reply, Bagg referred to the relation of the size of the tumour to the subsequent reaction to treatment. He pointed out that the solution diffused into different portions of the tumour causing more extensive reactions in some parts than in others. P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

CARDIO-VASCULAR DISEASES

Aetiology. The close relationship existing between syphilis and rheumatism in the production of cardio-vascular affections is emphasized by Minet, Duhot, and Legrand. In one group of cases syphilis represents the predisposing cause and acute articular rheumatism the determining cause. In a second group rheumatism is the fundamental disease on which syphilitic infection is grafted. A cardiac lesion which has hitherto remained latent rapidly becomes severe under the influence of superadded syphilis. In a third group the two infections—acute articular rheumatism and syphilis—exercise their injurious action simultaneously and extremely serious cardio-vascular lesions result. The writers are convinced that a large number of cases of cardiac and aortic disease are due to this double aetiology. One should therefore not be content with determining the syphilitic or rheumatic origin of aortitis or cardiac disease, but should ascertain, when one of these causes is evident, whether the other has not been overlooked.

Ophüls, of San Francisco, examined the records of 500 complete necropsies at the Leland Stanford Junior University School of Medicine in order to find proof of the suspected interrelation between certain infectious diseases and the later development of arteriosclerosis or of the syndrome of cardio-vascular disease. His results were as follows: (1) A comparison of cases in which all history or signs of previous infection were absent with those in which they had been detected showed that chronic arterial disease was almost entirely lacking in the first group and appeared early and very frequently in the second group: (2) this connexion did not exist in all infectious diseases, but was fairly well limited to chronic rheumatic (septic) conditions; (3) arteriosclerosis and associated conditions were very rare in chronic pulmonary tuberculosis, and even in syphilis were not very common, especially if those cases were deducted in which a chronic rheumatic infection was present as well as syphilis; (4) there was no direct relation between the extent and severity of the arterial disease and the amount of functional disturbance in the cardio-vascular system.

Galli declares that the importance of heredity in cardiac disease is not so widely known as it deserves to be, although the older writers such as Morgagni, Lancisi, Albertini, Corvisart, and others had drawn attention to it. He gives the genealogical tree of a family of four generations, consisting of 24 members, at least 9 of whom were subjects of disease of the circulatory system. In addition to the inheritance of actual disease there are two forms of cardiac inheritance to which Galli in 1908 gave the name of *endocardismus hereditarius* and *myocardismus hereditarius*. In such cases though the endocardium and myocardium are not actually diseased and do not present any pathological changes on examination, their functional capacity and resistance are less than in normal persons, so that relatively slight causes, which would have no effect on the normal individual, produce in them true cardiac disease. Galli has observed the occurrence of tachycardia in a father and his two sons, and alludes to a family described by Wenkebach, in which the mother and her four children were subjects of bradycardia, their pulse being often under 50 per minute. By a regular life and moderate and progressive physical exercise, these hereditary defects may be corrected, whereas an irregular life and excessive and prolonged physical exercise may give rise to severe and even fatal collapse. Such cases react badly to acute disease and are unsuited for the hardships and privations of active military service.

Minet, Lemaitre, and Auguste describe a family of five brothers and sisters aged from 51 to 62, four of whom had mitral stenosis and the fifth mitral insufficiency and aortic stenosis. The father and paternal grandfather had been sufferers from cardiac disease and the mother was tuberculous. The five cases had all had dyspnoea on exertion since childhood, two had had acute articular rheumatism, one at 18 and the other at 24, and a third had had chorea at 9. None of them, however, showed failure of compensation, but all presented cardiac hypertrophy, especially of the left ventricle, so that the writers suggest that in addition to familial cardiopathy there was a sort of familial predisposition to react to the cardiac lesions by compensatory hypertrophy.

Adlmühler has investigated the aetiology of 462 cases of acquired valvular disease of the heart at the First Medical Clinic at Munich with the following results: Polyarthritis including polyarthritis and chorea and polyarthritis and syphilis accounted for 49·5 per cent. of the cases, cases of doubtful or unknown aetiology for 21·8 per cent., and syphilis for 18 per cent. Of 91 cases of aortic insufficiency syphilis was the certain or probable cause in 68 or 74·7 per cent.—a much higher proportion than that reached by polyarthritis in any of the other valvular defects. Only a small number of cases of aortic insufficiency were due to arteriosclerosis (2·2 per cent.), and polyarthritis was present in only 11 per cent.

Dedichen points out that the uncertainty which still prevails as to the effect of violent strain on the heart is largely due to the fact that there is seldom reliable evidence about the health of the heart beforehand. This gap in the evidence has been partly made good by systematic examinations of all the competitors in the Norwegian 50 kilometre ski race, immediately before as well as after the race. Weight, height, apex-beat, cardiac dullness, heart-sounds, pulse, blood-pressure, and urine, are all investigated, and incidents such as cyanosis after the race are recorded. These records are entered on every competitor's case paper, and to all the competitors in the years 1914–1918, inclusive, questions have been addressed as to the occurrence of illnesses which might be associated with strain. No answers in the affirmative have been received. Of 226 competitors, 8 showed outward displacement of the apex-beat after the race, and in 2 cases the cardiac dullness had increased to the right. In 30 cases after the race there was a distinct inward displacement of the apex-beat, which before the race was marked by a vertical strip of plaster. In all the cases in which the apex-beat became more distinct after the race it was within the nipple-line. In none of the 8 cases with outward displacement of the apex-beat after the race was there any sign of cardiac failure; the condition of these men was quite as good as that of the rest. In some cases the pulse was quicker before the race than after, and some of the best competitors exhibited bradycardia. Some competitors were very cyanosed after the race or extraordinarily pale; the cyanosed men were usually in good condition in other respects. In a few cases the blood-pressure was as high as 160 mm. (systolic) before the race. After it the blood-pressure had increased by 10 mm. in one case; in a few it was unchanged, but in most it had fallen, pressures of 75 to 80 mm. being recorded. Only in a few cases were such low pressures as 50 mm. observed after the race, and in these the general condition was irreproachable. With regard to chest-measurements and vital capacity, the competitors with good height-weight proportions, big chest-measurements, and great vital capacity did the best times. Thus the most successful weighed 400–470 gm. per cm. of height, and the first 7 in one race had chest-measurements of 90–97 cm. and vital capacities of 4,200–5,100 c.cm. Dedichen concludes that these examinations, which have been made since 1883, indicate no direct injurious effects of athletics on the hearts of healthy young men above the age of 20.

Symptomatology. Considerable attention has recently been devoted to the subject of **subacute bacterial endocarditis**, otherwise known as endocarditis lenta, as will be seen from the papers by Boyd, Cotton, and Horder in Great Britain, Baehr and Lande and Libman in the United States, Achard and Rouillard, Debré, Fiessinger and Janet, and Lereboullet and Mouzon in France, Becher, Jungmann, and Münzer in Germany, and Schippers and De Lange in Holland. Horder regards the disease as fairly common, his investigations having shown that 1 in 200 patients admitted to the medical wards of a large general hospital suffered from it. Cotton found it in 8 per cent. of patients with signs of gross valvular lesions attending a special heart clinic. Becher, who calls it ‘war endocarditis’, states that the disease was unusually frequent in soldiers during the last year of the war and was still more prevalent in the following year. Jungmann's cases also consisted almost entirely of men who had taken part in the war and had suffered from protracted infections due to wounds and other causes. According to Debré 66 per cent. of the cases occur in patients aged from 15 to 30: a few cases, however, have been observed above 30, and also in children (Schippers and De Lange). While Horder states that the sex incidence is equal, Debré maintains that the disease is commoner in the female than in the male sex, owing to the relative frequency of streptococcal infections of genital origin in women.

The following varieties of the disease are described by Debré: (1) Apyretic form. The existence of very long periods without any rise of temperature has often been noted, but complete apyrexia appears doubtful. (2) Anaemic form, characterized by intense anaemia, the cardiac signs not appearing till late. (3) Haemorrhagic form. Endocarditis lenta is probably a frequent cause of chronic purpura. (4) Painful form, characterized by the appearance of painful nodules in various situations. (5) Nervous form, associated with cerebral and meningeal symptoms, of which the cases described by Lereboullet and Mouzon are examples. (6) Silent form, in which there are no stethoscopic signs to direct attention to the heart. (7) *Formes frustes*, in which the patients present multiple arthropathies, albuminuria and transient febrile attacks. Purpuric eruptions are frequent and the endocarditis is not discovered until the autopsy. (8) Latent form with a fulminating termination due to cerebral haemorrhage.

Horder describes four cardinal signs of the fully evolved disease, which in order of importance are multiple arterial embolism, endocarditis, isolation of a bacterium from the blood-stream, and fever. Cotton and Jungmann each lay much stress on clubbing of the fingers and enlargement of the spleen as features of the disease. The slowness of its course is characteristic.

According to Debré it does not last less than four months and persists for a year as a rule, sometimes two years, and even more.

Baehr and Lande emphasize the frequency of diffuse glomerulo-nephritis (acute glomerulo-nephritis and subsequent chronic diffuse nephritis) as a complication. In their series of 77 cases 9 patients, or about 11·5 per cent., died of uraemia due to this cause.

The prognosis is always grave, but whereas Cotton and Debré each maintain that the disease is always fatal, Libman has seen four complete recoveries in a series of 150 cases, and Boyd reports a case in which the patient a year after his attack won a cross-country championship.

In fatal cases death is due to uraemia, progressive anaemia, or embolism.

Reid, of Boston, points out the fallacy of considering a presystolic murmur as an infallible indication of **mitral stenosis**. He states that the early systolic murmur, sometimes wrongly termed presystolic, occurs in large hearts, and suggests that it is produced by an insufficiency of the mitral orifice or failure of the muscular contraction in approximating the margins of the opening. Reid suggests that owing to the physiological tendency of the heart to dilate as the primary effect of exercise or excitement the murmur occurring in early systole may sometimes occur in the normal heart after exercise or excitement.

Vaquez and Magniel record several cases illustrating the occurrence of functional pulmonary incompetence as a complication of mitral stenosis, which was first described by Graham Steell in 1896. The mechanism of this incompetence is of two kinds. It may be due to rise of pressure in the lesser circulation which gives rise to distension of the pulmonary artery, or it may result from a process of pulmonary endarteritis similar to the infective endocarditis so frequently met with in subjects of valvular disease. Its localization in the pulmonary artery is explained by the fact that infective processes involve by preference those regions which by reason of excess of pressure are liable to overwork. When the lesion is the result of a mechanical distension of the vessel the prognosis is much less grave than when it is due to infection.

Garland and White, of Boston, record nine cases of paralysis of the left recurrent laryngeal nerve associated with mitral stenosis which have occurred at the Massachusetts General Hospital during the last eight years, and have collected 61 other cases from literature, so that the condition is probably frequently overlooked. They agree with Fetterolf and Norris that the pulmonary artery must be an intermediate agent in causing pressure, and with Lian and Marcorelles that a thrombus or mediastinitis may occasionally be the responsible factor. Probably auricular fibrillation is an important additional factor, besides the increase in size of the auricle in mitral stenosis, because in auricular fibrillation the auricle remains ballooned out with the ready production of thrombi.

Amblard, who during the last two years of the war had the opportunity of studying several thousands of cases of real or imaginary heart disease in a cardiological centre, came to the conclusion that patients suffering from mitral stenosis were almost invariably subjects of inherited syphilis. Not only were the family history and the presence of other clinical signs in favour of this view, but the Wassermann reaction, which was examined in 165 cases, was more or less definitely positive in 128. Amblard maintains that specific treatment, started at the time the lesion is discovered, though too late to act on the lesion itself, may have a favourable effect on the other symptoms, the nature of which had not hitherto been recognized.

After alluding to the frequency of familial valvular disease, Sachs, of the Third Medical Clinic of Berlin University, gives a description of congenital mitral stenosis in twin girls aged 19 and their brother aged 24. The parents and another sister of the patients showed no abnormal heart signs. There were no other malformations or signs of degeneration in the family, nor was there any evidence of inherited syphilis. The three patients showed different types of the disease. The first had no disturbance of compensation, the cardiac condition being discovered accidentally during treatment for contusion of the knee. The second case was in the stages of failing compensation, and in the third case the cardiac lesion was well compensated but was complicated by glomerulo-nephritis and chronic nephritis.

Queyrat, Gandy, and Deguignand report a case of congenital mitral stenosis, probably due to inherited syphilis, in a man aged 22, presenting the following features of interest: (1) It shows that pure congenital mitral stenosis is not, as was for a long time believed, the exclusive appanage of the female sex. (2) Associated with the mitral stenosis was a very rare congenital anomaly, viz. dilatation of the pulmonary artery. Nothing revealed the lesion on auscultation apart from accentuation of the pulmonary second sound, but on screening the patient a well-marked dilatation was found.

Lutembacher (1), who records a case of **tricuspid insufficiency** due to pneumococcal endocarditis, draws attention to the frequent association of tricuspid insufficiency with pulmonary lesions. In one group of cases, viz. in chronic disease of the lungs, such as extensive sclerosis, emphysema, and chronic bronchitis, the pulmonary lesions precede the cardiac symptoms, which do not develop until later, the tricuspid murmur only appearing when oedema of the lower limbs, enlargement of the liver, turgescence of the jugular veins, and cyanosis, indicate insufficiency of the right ventricle. In a second group of cases the pulmonary lesions are obviously secondary to the cardiac lesions and do not occur till late. In a third group both pulmonary lesions and tricuspid insufficiency may be the result of some acute infection as in the case reported by Lutembacher.

Ribierre, discussing the diagnosis of tricuspid insufficiency, remarks that pulsation of the liver, which is generally regarded as pathognomonic, is an inconstant and often late sign which may be observed independently of right auriculo-ventricular incompetence, especially in complete arrhythmia. The second sign regarded as pathognomonic is a systolic murmur in the xiphoid region not conducted beyond the apex nor to the back. This murmur is most distinct in the rarest form of tricuspid insufficiency, viz. that due to endocarditis of the right auriculo-ventricular orifice. On the other hand, in the commonest form, viz. functional tricuspid insufficiency secondary to mitral lesions and insufficiency of the left ventricle in hypertension complicated by dilatation of the right heart, the xiphoid murmur is inconstant and often difficult to distinguish from the concomitant murmur of mitral insufficiency. Ribierre concludes that there is not a sign or even group of signs pathognomonic of tricuspid insufficiency, the diagnosis of which can only be established by a consideration of the aetiology, symptoms and physical signs.

Bonnamour and Chapuis record a case of congenital **tricuspid stenosis** in a woman associated with mitral stenosis and aortic stenosis remarkable for the fact that the patient survived to the age of 54, whereas the survival of patients with congenital tricuspid stenosis usually does not exceed the age of 32, when, as in this case, the stenosis only admits one finger, or 42 when it admits two fingers.

From observations on 24 cases of well-marked **aortic incompetence** Williamson comes to the conclusion that although higher systolic readings in the leg than in the arm are found in the majority of cases of aortic incompetence, there is a large minority in which this is not the case. He suggests that the cause of the higher systolic reading in the leg is the commonly associated condition of hypertonic contraction or hypertrophy of the muscular coat, with or without accompanying sclerotic changes, which occùr independently of aortic incompetence.

Gallavardin (1), who records eight illustrative cases, describes a form of **aortic stenosis** in young adults with very distinct physical signs which is distinct from congenital stenosis, is not of arterial origin, nor of rheumatic nature. As a rule it is an isolated lesion, and, even when it is accompanied by slight insufficiency, stenosis is always the predominant lesion. It is not until an advanced stage that functional symptoms arise, and in some cases disturbance of development has been noted. The real nature of the affection is still doubtful. In some cases it may possibly be a congenital lesion which has been late in manifesting itself, but in most cases it is probably an acquired lesion which has developed slowly in childhood or adolescence, as the result of subacute or chronic endocarditis due to some as yet undetermined cause. In its tendency to be an isolated lesion, its appearance in early life, absence of rheumatic aetiology, prolonged latency, and obscure nature, it resembles the mitral stenosis of Duroziez.

Herrick makes the following classification of cases of **coronary thrombosis** based on clinical symptoms: (1) Cases of instantaneous death in which there is no death struggle, the heart-beat and breathing ceasing at once. (2) Cases of death within a few minutes or a few hours after the obstruction. (3) Cases of severity in which, however, death is delayed for several hours, days, or months, or recovery takes place. (4) A group that may be assumed to exist, embracing cases with mild symptoms, e. g. a slight precordial pain usually not recognized, due to obstruction in the smallest branches of the arteries.

According to Lutembacher (2), sudden death in heart disease is usually due to cardiac thrombosis, as the thrombi which sometimes develop in the infected cavities are too large to be carried into the circulation and give rise to distant emboli, but are suddenly caught in the auriculo-ventricular orifices or large vessels of the base. Death may occur without any apparent cause, or on the other hand may coincide with some therapeutic measure, such as administration of a cardiac tonic, which should therefore be given with prudence. Apart from cardiac thrombosis sudden death may occur in angina and in subjects of aortic disease, after injections of mercury or arsenobenzol.

From a study of 100 cases of true **angina pectoris** Gallavardin (2) came to the following conclusions: (1) True angina pectoris is incomparably more frequent in men than in women, 93 of his cases being in men and only 7 in women. It is also much commoner in private than in hospital practice, only two of his cases being in hospital patients. (2) As regards age, the affection may in exceptional cases appear below 40 (4 per cent.), 24 per cent. were under 50, 47 per cent. were between 50 and 60, and 29 per cent. over 60. (3) Syphilis, though a very important cause of angina pectoris (vide *Medical Science,* 1920, **1**, 480), is far from being the only factor. In 91 cases in which the presence of syphilis could be thoroughly investigated, syphilis was certain in 32 per cent. and doubtful in 5 per cent., while there was no evidence of it in 63 per cent. Even allowing for errors it does not appear likely that syphilitic infection was responsible for more than half the cases of true angina pectoris. On the other hand, out of 14 cases in which angina pectoris was associated with aortic incompetence, syphilis was certain in 13. Gallavardin concludes that though true angina pectoris is not due to syphilis in more than half the cases, when associated with aortic incompetence, it is almost always of syphilitic origin.

According to Bard, of the Strasbourg Medical Clinic, who reports an illustrative case, no previous writer has drawn attention to the relation between Raynaud's disease and angina pectoris except Duroziez, who, in 1874, and again in 1884 and 1891, maintained that angina pectoris was closely related to local asphyxia, and was as frequently due to a neurosis of the peripheral nerves as to a cardiac lesion. Bard reports a fatal case of angina pectoris associated with Raynaud's disease in a man aged 33. The X-rays showed an absence of cardiac and aortic lesions and there was no history of syphilis. No autopsy, however, was obtained.

Lutembacher (3) draws attention to the grave prognostic significance in angina pectoris of a sudden fall of blood-pressure which may drop from 25 or 28 to 8 or 9. It is rare for this fall to occur at the beginning of an attack, but it usually does not take place until after several hours of intense pain. A gradual fall of blood-pressure is as bad a prognostic as a sudden fall. The patient complains of suffocation, which is not due to pulmonary oedema, but is connected with the extreme acceleration of the heart, the beats being 150 to 200 in a minute, feeble and unequal, and not transmitted to the pulse. Death from syncope soon takes place. The anatomical substratum of this syndrome has still to be determined, but there is probably a sudden dilatation of the cardiac muscle.

Under the name of **dyspragia cordis intermittens**, Bittorf, of the Breslau University Medical Clinic, describes a condition resembling angina pectoris but differing from it anatomically and in its functional manifestations. Men, especially of advanced age, are more frequently attacked than women. Usually the disease appears at the end of the fifties or in the sixties. Syphilis plays no part in the aetiology, but alcoholism and abuse of tobacco are very important if not the chief causes of the condition. The prognosis, unlike that of true angina pectoris, is favourable. Considerable improvement may occur, and Bittorf has not seen a fatal case. Owing to the absence of post-mortem evidence the underlying anatomical condition is not established, but arteriosclerosis with involvement of the coronary vessels is obviously present. After rapid walking out of doors the patient complains of a feeling of pressure in the cardiac region, which increases on further effort. The pain, which at first is localized in the cardiac region, passes round the thorax or up to the neck, and a feeling of irritation, weakness, and numbness occurs in the left arm. In some patients sweating takes place during the attack. There is no dyspnoea, however, and the patient's outward appearance is not changed. Apart from a slight slowing there is no change in the pulse. If the patient stands still at the commencement of an attack, the symptoms subside in one or two minutes. The attack never occurs at rest or in bed, nor is it ever caused by slow, regular movements. Treatment consists in immediate rest and the administration of nitroglycerine. The patient should accustom himself to walking slowly and should avoid all unnecessary effort or nervous excitement. The meals should be small and frequent, spiced foods and drinks containing carbon-dioxide should be avoided. Potassium bromide and moderate doses of potassium will prove useful.

Martens states that **spontaneous rupture of the heart,** as distinct from traumatic rupture, on which there is an extensive literature, has received comparatively little attention owing to the rarity of its occurrence, the impossibility of diagnosis, and the failure of treatment of any kind. Various causes are responsible for the condition. The most frequent is fatty degeneration, which was found in 77 cases of rupture of the heart collected by Quain, who also found rupture of the heart in 28 out of 83 cases of fatty heart or in 34 per cent. After fatty heart came myocarditis and occlusion of a coronary artery followed by abscess of the heart wall, cardiac aneurysm, and myomalacia cordis, while tumour, gumma, and echinococcus disease of the heart may be mentioned as rare causes. The occurrence of spontaneous rupture is favoured by one or more violent efforts or emotion. About two-thirds of all the cases occur above the age of 60, but no period of life is exempt. Schaps saw a case in a child of four months. The left ventricle is most frequently attacked, in which, according to Legg, 59 out of 60 cases of cardiac aneurysm occur. Although a single rupture, seldom larger than 1 cm., is the rule, multiple ruptures sometimes occur. The symptoms are pain in the cardiac region, anxiety, cyanosis, collapse, and signs of haemorrhage. Usually death occurs in a few hours, but in some cases the symptoms have lasted 11 or 17 days. In Marten's case, which occurred in a man aged 70, the patient survived two days. One complete rupture was found in the left ventricle, and there were also two incomplete ruptures. The heart-muscle was very brittle and a microscopical examination showed marked fragmentation of the fibres.

Weltmann records a case of a **cardiac tumour** in a woman aged 20, who was mentally and physically a degenerate, and had been subject from childhood to respiratory catarrh. The symptoms were those of isolated tricuspid stenosis with progressive cardiac insufficiency associated with attacks of Adams-Stokes disease. The necropsy showed a lobulated tumour in the right auricle, which an histological examination proved to be a pseudo-myxoma.

Macfie and Ingram record three cases of **cardiac aneurysm** in native boys of the Gold Coast, aged 7, 6, and 12 years respectively. Death was sudden in all three cases, and, so far as could be ascertained, was not preceded by any symptoms of illness. Two of the boys died from rupture of the aneurysm into the pericardium. In all three cases the coronary arteries showed a slight degree of endarteritis with some degeneration of the inner coat. No other naked-eye lesions could be discovered, but the writers are confident that all the boys had previously suffered from malaria, a disease from which no child on the Gold Coast escapes, and suggest that the coronary endarteritis in these cases was due to malaria.

According to Lutembacher (4), who records three cases, aneurysms of the left ventricle are not discovered until after death, and are generally regarded as having no clinical interest. It is not so much that they remain latent, but their symptoms tend to be confounded with those of the cardio-vascular lesions with which they are associated. In spite of their size they do not show any tendency to form pulsating tumours in the front of the chest wall or below the costal margin, probably owing to the fact that they are drawn downwards by their own weight. They become embedded in the diaphragm or liver, where they are invested with pericardial adhesions and so escape detection. The only symptom of any value which Lutembacher has found is localized pain at the apex which is apparently due to deep-seated lesions occurring in the wall of the heart and is often very violent. As a rule, however, it is dull in character and may even be reduced to a feeling of weight or discomfort in the chest. The development of pericardial symphysis localized to the apex accompanied by signs of cardiac insufficiency gives rise to a syndrome which is of diagnostic value when present apart from any cardio-vascular lesion. Contrary to what is observed in rheumatic pericardial adhesions in which the myocardium contracts vigorously and draws with it the wall of the chest, depression of several ribs and systolic retraction of the apex are not observed. The apex-beat is even indistinct although the myocardium as a whole contracts vigorously. This suggests that the localized reaction of the pericardium is accompanied by a severe destructive lesion of the myocardium. Cardiac insufficiency is manifested by dilatation of the left auricle and ventricle, a functional mitral murmur, and severe dyspnoea.

According to Müller, jun., of the Zurich University Medical Clinic, cases of **paroxysmal tachycardia** may be divided into those whose principal cause lies in the heart and those which are determined by disease of the central nervous system. The existence of paroxysmal tachycardia originating in the vagus or sympathetic has not yet been proved. If this classification is correct, the treatment must vary accordingly. Some cases will react to drugs which act on the heart, such as quinine, quinidine, physostigmine, and digitalis, and others to remedies which act on the central nervous system, such as the faradic current, bromide, and morphia. Lastly, in some cases cardiogenic and central causes may be combined.

Yacoel adopts the following classification of the varieties of paroxysmal tachycardia: (1) The complete or ventricular form (Bouveret-Hoffmann's disease) which is subdivided into nodal, supranodal, and infranodal forms. (2) The partial form known as 'auricular flutter', of which three varieties are described accordingly as it is regular, slightly irregular, or completely irregular.

Muschalik reports two cases of paroxysmal tachycardia during labour in two previously healthy women, aged 23 and 34 respectively, with no cardiac disease, the pulses during the attacks being 160 and 140 apart from any obstetrical trauma.

Willius, in a study of 277 patients with **bradycardia** in which the upper limit of the pulse-rate was 60, divides the cases into three groups: (1) those with myocardial disease, with or without lesions of the auriculo-ventricular bundle, (2) endocardial valvular disease, (3) vagus augmentation.

Brachman, from examination of 400 cases of **auricular fibrillation** in patients aged from 16 to 76, came to the following conclusions: (1) The three most constant and diagnosable signs in auricular fibrillation are (*a*) the irregular irregularity in rhythm, (*b*) enlarged transverse diameter of the heart, (*c*) a difference in the apex- and pulse-rate. (2) An irregularly irregular heart rhythm which is almost pathognomonic of auricular fibrillation. It must be differentiated from that found in (*a*) multiple premature beats, especially those of auricular origin and (*b*) sino-auricular heart-block. (3) There are no symptoms pathognomonic of auricular fibrillation, nor are there any much more suggestive of this than of any other cardiac condition. (4) The commonest antecedent cause is rheumatic fever. Rheumatism or chorea was found in 39 per cent. of the total number questioned, and 19 per cent. gave a history of no previous illness. Graves's disease leads very definitely to auricular fibrillation. (5) There is no predisposition in either sex to auricular fibrillation. (6) Primary myocardial involvement was found in as many cases as were associated with pure mitral stenosis. The other conditions in order of frequency were mitral regurgitation, both mitral and aortic disease, and aortic disease alone. (7) As the pulse-rate usually does not give the ventricular rate of contraction the apex-beat must be counted as well in all cases of auricular fibrillation. (8) The chief therapeutical agent is rest—physical, mental, and cardiac.

Goodall records 20 cases of **heart-block**, 15 of which were in males and 5 in females; their ages ranged from 4 to 74 years. The main features in these cases were: (1) The relative infrequency of a rheumatic or syphilitic history. (2) The almost invariable association of the condition with mitral regurgitation. (3) The tendency to sudden death on gastric distension or exertion. (4) The occurrence of Stokes-Adams 'fits' when the heart-block is complete. (5) The frequency of pain as a symptom. (6) The possibility of the condition being transmitted from mother to child. (7) The ability of some patients to work and even to stand severe operations.

Carter and Howland report a case of congenital complete heart-block in a girl aged 10, and state that there are only seven other cases on record in which the diagnosis has been confirmed by graphic records. A histological study does not appear to have been made in any of these cases. The remarkable features in the present cases were the diagnosis of the cardiac murmur at 9 months of age, an evidence of the existence of congenital malformation of the heart, the confirmation of the clinical diagnosis of heart-block by electro-cardiographic records at the age of 3, the history of having passed successfully through an attack of pertussis at the age of 5, and the child's normal appearance at the age of 10.

Vetlesen, a physician attached to Ullevaal Hospital in Christiania, gives an extraordinarily detailed autobiography, tracing the course of his own heart symptoms since they began, at the age of 60, in 1912. The salient features of his case, which he did not submit to cardiographic examination, were recurrent attacks of arrhythmia with giddiness, culminating on some occasions in complete loss of consciousness. There was no sign of dilatation of the heart or of valvular disease, the blood-pressure was 140, there was no history of rheumatic fever, syphilis, or septic infection, and the only aetiological factor of importance was overwork for several decades. He seems to have tried practically every cardiac drug in the pharmacopoeia without benefit. On December 25, 1919, after an attack of arrhythmia had lasted over 2 months, he began taking quinidine in pills of 0·1 gm. The arrhythmia promptly ceased, but he had overdosed himself with 12 pills a day, and he suffered from abdominal pain, nausea, headache, and a slight rise of temperature. After changing the dosage in different ways, he found that with 6 pills a day, taken 2 at a time, he could control his arrhythmia to a remarkable degree. Up to May 1920 there had been only a few abortive attacks, and others, adumbrated by prodromal symptoms, did not materialize. In the absence of arrhythmia or prodromal symptoms, it was not necessary to take as many as 6 pills a day.

Lyter, of the St. Louis University School of Medicine, has made a study of 30 cases of **pericardial adhesions** of various grades met with among 514 consecutive autopsies at the St. Louis City Hospital. He divides pericardial adhesions from the aetiological standpoint into three classes: (1) the tuberculous; (2) those resulting from an attack of acute pericarditis or more probably pancarditis complicating some acute infectious disease, such as rheumatic fever, tonsillitis, pneumonia, typhoid, &c.; (3) cases without any history of previous acute infections. The adhesions in this class were probably the result of long and continued injury to the pericardium from chronic infections or some unknown intoxication. Lyter considers that Pick's syndrome of chronic pericardial adhesions, chronic mediastinitis, capsular cirrhosis of the liver, and chronic peritonitis with ascites is merely a very advanced type of this group.

Achard discusses the occurrence of **transient paralysis in cardiac patients**, to which he first drew attention in 1897 in conjunction with Léopold Lévi. The paralyses may occur in cardiac patients during or apart from asystole and also in subjects of arterial hypertension. Similar paralysis may be met with in various morbid conditions, such as Bright's disease and cirrhosis of the liver. The following causes are responsible: (1) stasis which gives rise to oedema, distension of the perivascular space, and small extravasations of blood within this space; (2) ischaemia due to narrowing of the arterial lumen by sclerosis aggravated by spasm. Toxic factors, especially in Bright's disease or cirrhosis of the liver, may play some part in the production of these paralyses, but are not so important as circulatory disturbances. The prognosis does not depend upon the paralysis but on the state of the heart and circulation. Treatment, therefore, should be directed not to the nervous system but to the overloaded condition of the right heart, the pulmonary stasis, and the resulting oedema.

O'Hare emphasizes the importance of differentiating **vascular hypertension** from chronic nephritis. The patient with vascular hypertension can be recognized clinically by his healthy appearance, lack of renal symptoms, and by physical and laboratory examination, especially by tests of renal function. The urinalysis of 25 cases of vascular hypertension is given, showing that though albumin and casts occur about as frequently as in chronic nephritis, the maximum specific gravity is much higher than in the nephritis patient. In other words, the kidney of vascular hypertension maintains its ability to concentrate in contrast with the nephritic kidney. Moreover, the functional tests show but little renal impairment in vascular hypertension as compared with chronic nephritis.

During the last few years Hitzenberger and Richter-Quittner have made a systematic examination of the blood-sugar in a number of cases of vascular hypertension which they divide into three groups: (1) primary hypertonus; (2) secondary hypertonus due to chronic glomerular nephritis; (3) hypertonus associated with diabetes mellitus. They found that the hyperglycaemia, which was a regular occurrence in primary and secondary hypertonus, differed from that met with in diabetes mellitus in being independent of an alimentary factor. It was therefore not due to a disturbance of sugar assimilation but to a persistent over-production of sugar. In cases in which vascular hypertension was associated with diabetes mellitus hyperglycaemia increased out of proportion to the excretion of sugar. Vascular hypertension was also frequently found to be accompanied by hyperuricaemia. The writers suggest that the syndrome of hypertension, hyperglycaemia, and hyperuricaemia depends on an increase in the secretion of adrenalin.

According to Lian and Boulot, pulsus alternans is frequent in hypertension accompanied by signs of cardiac and renal insufficiency. In the course of four months they found ten examples at the out-patient department of a general hospital among 64 cases of hypertension examined during this period. It is easily recognized on clinical examination. Although it is generally regarded as a bad prognostic, the present writers, like Gallavardin and Gravier, assert that such cases usually survive for two or three years and sometimes longer. Temporary disappearance of pulsus alternans under treatment is a favourable sign. Treatment consists in administration of cardiac tonics, such as digitalis or ouabain, strict diet, diuretics, purgatives, and blood-letting, so as to combat renal insufficiency.

In a paper on high blood-pressure and life assurance, Weber suggests that after a single examination at which the brachial systolic blood-pressure is found to be as high as 200 mm. Hg in a person whose urine is free from albumin and sugar, and whose heart is not greatly enlarged, and who otherwise appears healthy, the applicant's age should be regarded as 70 when in reality it is under 50. This might be modified if, on further examination and prolonged observation, the blood-pressure is found to be often much lower and the results of ordinary hygienic treatment prove quite satisfactory.

Meyer, of New York, ascribes **thrombo-angiitis obliterans** entirely to tobacco poisoning in patients with a predisposed nervous system. All his patients were Russian-Polish Hebrews, who, as the result of centuries of persecutions, were neurasthenics by heredity. The functioning of the eliminating glands innervated by the sympathetic, viz. the kidneys, intestines, and other glands which secrete to the surface, is probably subnormal in such cases. Meyer maintains that the only real cure for the condition is prophylaxis, and recommends that people so constituted as the Hebrews should not smoke.

Bernhard carried out the blood-sugar tolerance test on 36 verified cases of thrombo-angiitis obliterans with the following results: (1) The blood-sugar concentration at the zero hour varied between 96 and 2,110 mgm., with an average of 115 mgm. per 100 c.cm., the urine showing no sugar at the zero hour. (2) The blood-sugar at the end of the 45-minute period varied between 106 and 344 mgm. with an average of 179 mgm., and 36 per cent. showed sugar in the urine at the 45-minute period, of which 23 per cent. had a lower blood-sugar concentration than 150 mgm. Six cases had a blood-sugar concentration of 180 mgm. or higher without showing sugar in the urine, and 69 per cent. showed a concentration of 150 mgm. or more. (3) The blood-sugar at the end of the two-hour period varied between 96 and 288 mgm. with an average of 146 mgm. 33 per cent. showed sugar.

Beneke has recently seen three fatal cases of arterial diseases which he attributes to nicotine poisoning. All three patients, soldiers aged 42, 44, and 48 respectively, had been extremely heavy smokers, they had shown no signs of alcoholism or syphilis, and no history of any other infection was obtainable. In two death was due to disease of the coronary arteries and in one to suicide. In each case there was a well-marked fatty degeneration of the intima of the coronary arteries and to a less extent of the carotid, subclavian, axillary, mesenteric, and iliac arteries. In several places sclerosis of the intima was associated with fatty degeneration, but it was never the predominating feature. Calcification was absent.

Martinet (1) records his observations on 29 cases of **aortic aneurysm**, 25 of which occurred in civil practice among 4,000 cases of mostly chronic disease or 1 in 160 cases and 4 in military practice or 1 in 271 cases. He thinks it probable that a large number of aneurysms pass unrecognized and that a considerable number would be detected by systematic radioscopy. Twenty of his cases were in men and 5 in women. All the patients were aged between 40 and 68. Among his 25 civilian cases syphilis was certain in 16, doubtful in 5, and in 4 was almost certainly absent. In 2 of the 4 military cases it was certain, in 1 doubtful, and in 1 almost certainly absent. As regards the causation of non-syphilitic aneurysm, malaria, gout, acute articular rheumatism, and especially alcoholism, have been incriminated without it being possible to establish a very definite relation of cause and effect. Martinet, however, is convinced that a certain number of non-syphilitic aortic aneurysms do exist, and refers to the occurrence of aortic aneurysm in animals, especially the ox, less frequently the horse, and, in exceptional cases, the dog.

Du Bray, of the University of California Medical School, reports a case of saccular aneurysm of the descending thoracic aorta with direct rupture into the lower lobe of the left lung and the left pleural cavity in a man aged 50. The physical signs were misleading, and the diagnosis was made of massive haemorrhage into a bronchus in ulcerative pulmonary tuberculosis. Du Bray points out that haemoptysis should be regarded as a symptom of thoracic aneurysm as well as a symptom of other thoracic diseases, such as tuberculosis, mitral stenosis, and mediastinal tumours, and that it may be frequent and persistent before a fatal haemorrhage occurs.

Diagnosis. A new diagnostic method in cardiac disease is recommended by Tornai, who remarks that as a general rule a murmur caused by a valvular defect is all the more distinct: (1) the larger the volume and the greater the rapidity of the blood passing through the cardiac orifice, and (2) the nearer the cardiac orifice is to the anterior chest wall or to the site of auscultation. A ventral or thoracic decubitus is the position in which the heart and great vessels come closest to the anterior chest wall, and in this position the cardiac chambers are best filled. Auscultation can be best carried out by making the patient assume the 'knee-elbow position' or support his body on both knees and palms, keeping the thorax in as horizontal a position as possible. If for any reason it is impossible for the patient to assume this position, he should be made to bend forward as much as possible, when the heart-sounds are heard more distinctly than in any other position, if not so clearly as in the 'knee-elbow position'. Another advantage of this position is that it can at once be determined whether the heart is hypertrophied or not. This question is of special importance when one wishes to discover whether the patient is suffering from a cardiac neurosis or whether some serious mischief is present. It is important that a very short stethoscope should be used and should be applied perpendicularly to the point auscultated.

Prognosis. According to Friedländer, of Breslau, who reports two examples in girls aged 10 and 13, in addition to instances related by earlier writers such as Jaksch, Gerhardt, Beneke, Lewinsky, Fräntzel, &c., there are a number of convincing cases published by recent writers such as Castiaux and Langier, Leyden and Senator, of a complete cure of a valvular lesion. In Friedländer's cases, in addition to pericarditis, there was evidence of mental insufficiency and aortic disease. In both cases, however, the signs of aortic disease disappeared, and X-ray examination showed a heart of the typical mitral type.

Commenting on Friedländer's cases, Aufrecht, of Magdeburg, alludes to a case which he published in 1869 of aortic insufficiency in which, in spite of the loss of a whole valve, the process was found to be healed at the autopsy, water poured into the aorta being retained in the valves, only two of which were present but were freely movable though much enlarged and thickened. Aufrecht also describes two cases in which mitral insufficiency followed acute articular rheumatism in boys at the ages of 5 and 12. Both presented enlargement of the heart and a very loud systolic murmur which persisted for several months. A year later no signs of cardiac disease could be found. Both cases are now aged between 45 and 50 and are in good health. The prognosis of heart disease therefore is not necessarily unfavourable.

Treatment. Levy, of the Hospital of the Rockefeller Institute of Medical Research, has collected from the literature of the last three years reports of 101 cases of auricular fibrillation treated with quinidine, in 59 or 58·4 per cent. of which the normal rhythm was restored. The duration of the effect was usually short, ranging from a few days to a month. The longest period was four months. The usual dosage was 0·4 gm. by mouth three times a day before meals. Regularization of the rhythm usually occurred on the second or third day of treatment. Unpleasant effects such as palpitation, headache, diarrhoea, nausea, and vomiting were occasionally observed. Tachycardia usually preceded the onset of normal rhythm. Electro-cardiograms made while the heart-rate was still rapid showed in some instances the presence of auricular flutter as the transitional mechanism.

Drury and Iliescu treated 13 cases of auricular fibrillation with quinidine sulphate and in six cases the normal rhythm was re-established, while in the remaining seven, although similar changes were produced in the retardation of the auricular rate, the movement persisted without break and the rate returned on withdrawal of the drug to its original level.

Lewis, Drury, Iliescu, and Wedd describe the action of quinidine sulphate on the fibrillating auricle as perhaps one of the most remarkable and dramatic which is known to therapeutics. The essential feature of the reaction is an invariable and conspicuous reduction of the rate at which the auricle beats. The writers emphasize the fact that quinidine sulphate is a remedy of which we have still too little knowledge, and is one which, unless it is controlled by frequent records of the auricular and ventricular action, is not without serious risk. They conclude that the time has not yet come when its use in general practice may be advocated.

Martinet (2) (3) recommends the administration of cardiac extract in constitutional myocardial debility and acquired myocardial degeneration. One or two teaspoonfuls of powdered peptonized extract of ox heart are given daily by mouth, or rectum three times a week, or ten days a month, the average dose corresponding to 30–100 gm. of the fresh organ. The success of the treatment which was shown in three-quarters of Martinet's cases was manifested by rise of the differential pressure, increase of power of the myocardial reserve, increase of diuresis, reduction or progressive disappearance of oedema and dyspnoea, diminution of cardiac dilatation and attenuation or disappearance of symptoms of angina.

Barringer, of the Cardiac Clinic of the New York Hospital, maintains that physical exercise not only increases the resistance to general infection of patients with heart disease exactly as it does in the case of normal persons, but also in all probability makes the heart itself more resistant to reinfections. The exercise may be energetic or mild. The energetic type, which includes exercise with dumb-bells, stair-climbing, skipping-rope, running, hopping, and calisthenics, produces an increase of blood-pressure of between 20 and 40 mm. Hg, should not cause excessive dyspnoea, and should be followed by a normal curve of systolic pressure. The mild form of exercise, of which walking, croquet-playing, and dancing, limited to one-step, are examples, stimulates the heart's activity, but moderately over long periods of time, as shown by the small increase of blood-pressure following the exercise. This form of exercise should be used for patients with small cardiac reserve and also to supplement the more energetic type.

Wilson, who has made observations on 71 school children with definite organic heart disease without symptoms of insufficiency, found that 69 per cent. had a normal tolerance for standardized test exercises, 29 per cent. had fair tolerance, and 2 per cent. had a poor tolerance. She is of opinion that exercise tolerance tests give valuable information for the regulation of the activities of a child with heart disease and that fear of exercise in such cases is unwarranted.

According to Macht benzyl benzoate is a powerful vasodilator without being depressant to the heart when administered by mouth in small doses. Owing to this property it has been found effective in the treatment of hypertension and angina pectoris. The best method of administering the drug in such cases is in alcoholic solution which admits of rapid absorption and a control of the dose. Macht gives a 20 per cent. alcoholic solution by mouth, either in cold water or milk, in doses of 20 or 30 drops three or four times a day. The drug was given to some patients repeatedly for over a year without producing any toxic symptoms. The indications for its use are precisely the same as those of other vasodilators, such as the nitrites.

Laubry and Mougeot have studied the action of benzyl benzoate both in normal persons and in patients with hypertension. In the former its action was inconstant. Though a few showed a fall of 3 cm., in the majority the blood-pressure was not affected, showing that a healthy organism is able to adapt itself to vasodilatation. In hypertension, on the other hand, a fall of blood-pressure as determined by Pachon's oscillometer was the rule, and ranged from 1 to 3 cm. It began about half an hour after taking the drug, became more pronounced at the end of 45 minutes, and lasted 1½ hours. The prolonged action of the drug was studied by giving it three or four times a day. No bad local or general effects were noted, and a rise of pressure was never obtained. Fall of blood-pressure was not constant, but was all the more frequent and pronounced the further removed the hypertension was from the stage of decompensation. The drug usually failed to act in hypertension complicated by aortitis, nephritis, or insufficiency of the left ventricle. In addition to change in the blood-pressure benzyl benzoate produced improvement in the symptoms, causing disappearance of obstinate headache, vertigo, numbness, and vascular pain. It seemed to cause some relief in angina pectoris, but its action was less marked than that of amyl nitrite or trinitrin. The hypotensive action of the drug lasts several days, and at the end of the week the doses may be reduced to a quarter of their original size. Stopping the drug is not followed by a reaction but only by a return of the blood-pressure to its original level.

According to Allen, who records 20 illustrative cases, in some cases of hypertension the mere restriction of the overload of salt and water brings relief which is comparable to the benefits of diet in diabetes. A very close restriction of water may be impracticable at the beginning of treatment because of the salt stored in the patient's body and the inadvisability of imposing any real suffering from thirst. Moreover, in many cases no rigid fluid restriction is necessary, and moderate quantities may be actually beneficial for flushing out salt or nitrogen. The benefits of chloride restriction consist in making the patient more comfortable, diminishing the danger of apoplexy, and possibly checking the progressiveness of the disorder. By far the best results are obtainable in the earliest cases when the hypertension is intermittent rather than continuous.

For the last three years Steel has employed intravenous injections of 2 per cent. solution of sodium citrate every second day for a month and every third or fourth day for the second month in the treatment of thrombo-angiitis obliterans. Daily leg massage is given and the patient is put in a wheel-chair with his feet hanging down a short time each day. Increased walking is permitted as the symptoms subside and evidence of a functional collateral circulation appears. Potassium iodide in 10 gr. doses t.d.s. is given throughout the whole course of treatment. The effects of treatment in six cases in which Steel employed this method were: (1) relief of pain after the second injection, (2) checking of the gangrene and spontaneous amputation of dead tissue, (3) healing of indolent painful ulcers, (4) slow but sure establishment of collateral circulation.

Eight cases of intermittent claudication treated by diathermy are reported by Grünbaum. Improvement took place in all, and in some instances the patients were able to walk long distances free from pain. Each sitting lasted 10–20 minutes, the strength of the current varying between 400 and 800 milliampères. The treatment was continued for from four to eight weeks.

Bamberger relates a case of intermittent claudication successfully treated by quinine bisulphate in doses of 0·2 gm. t.d., subsequently increased to 0·3 gm. t.d., a total of 6·0 gm. being given. The treatment was suggested to him by the favourable results obtained by van Bergmann in angina pectoris with quinidine, and the success of the drug in intermittent claudication is attributed by Bamberger to its relaxing the spasm of the arteries of the leg.

Scheffler, Sartory, and Pellissier have been moved to try the intravenous administration of sodium silicate by consideration of the very large amount (90 per cent.) usually lost by other methods. Proceeding with all due precautions they determined the lethal dose for animals and then commenced with very small doses in human beings. They now use a 0·005 gm. per c.cm. solution. Of this they give 2 c.cm. every alternate day for six injections. The course is repeated or continued as required. With this dose they have had no suggestion of any ill results. The cases treated have been chiefly elderly persons affected with angina or with other symptoms of arteriosclerosis. The authors claim that reduction of blood-pressure, although often effected, is not the only result of using this drug by the intravenous route, and call particular attention to the increase of that sense of well-being which is so important to the patient.

Hare, who had previously recorded 30 cases of sacculated aneurysm of the aorta treated by wiring and electrolysis (vide *Medical Science*, 1920, **2**, 222), reports three more cases in which the results were excellent. One of the most important effects of the operation is the relief of pain which occurs almost at once in every case.

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DIABETES INSIPIDUS

Aetiology. According to Schulmann and Desoutter diabetes insipidus is commoner in men than in women, 58·6 per cent. of the cases occurring in the male sex according to Marañon, and 64 per cent. according to the writers' own statistics. They suggest that this predominance of the disease in men is due to syphilis, which is often responsible for the syndrome and is more frequent in the male sex. 85 per cent. of the cases develop before the age of 20 (Marañon). Sometimes the symptoms appear very early. Thus Cozzolino has reported a case in an infant of two months and Diluca in one of three months. It seems as if the hypophysis had a marked functional instability in childhood and at puberty. Diabetes insipidus may also be observed in old age. Heredity is an important predisposing cause. Thus fourteen cases of diabetes insipidus occurring in four generations except the second, in which apparently no member was affected, are reported by Janzen and Broekman, of the Utrecht Medical Clinic. Contrary to the general rule, four of the cases were males and ten females. A similar pedigree was published by Weil senior and Weil junior, of Heidelberg, of five generations consisting of 220 persons, of whom 35 (21 men and 14 women) were sufferers from diabetes insipidus. Janzen and Broekman have also collected 11 other cases of hereditary diabetes insipidus from the literature published by Oris, Pain, Gee, Marinesco, Lauritzen, McIlraith, Sasse, Clay, Lacombe, Hewson, and Lancereaux respectively. The symptoms first appear in infancy, sometimes later, become more pronounced about the twenty-fifth year, and then diminish. The abundant excretion of water has no effect upon the heart, and generally speaking the subjects of hereditary diabetes feel quite well, are able to follow their ordinary occupation, and reach old age. Weil senior is of opinion that the hereditary form of diabetes insipidus should be separated from the acquired form. In the cases described by Janzen and Broekman, however, there were no distinguishing features apart from heredity. Weil suggests that there is a difference in prognosis, but as the Dutch writers point out, in many cases of diabetes insipidus in which cerebral tumour, cerebral syphilis, and tuberculous meningitis can be excluded, the prognosis is also favourable.

The immediate causes of diabetes insipidus according to Schulmann and Desoutter are as follows: (1) Traumatism. By acting directly or indirectly trauma doubtless produces intraparenchymatous haemorrhages which are sufficient to vitiate the pituitary secretion. The haemorrhages may subsequently be absorbed, and this would account for the transient character of some cases of post-traumatic diabetes insipidus. (2) Tumours. These are a frequent cause of diabetes insipidus and may be malignant or innocent, cysts, gummata, &c. Metastases from a mammary epithelioma are relatively common. (3) Infections. All infections may attack the hypophysis and give rise to polyuria, especially syphilis and tuberculosis. (4) Intoxications. In this group pregnancy is included, in which the anterior lobe of the hypophysis undergoes certain changes. (5) Emotions. In contrast with exophthalmic goitre, in which emotion causes secretory hyperactivity, in diabetes insipidus the result of the sudden emotion is a functional deficiency of the organ.

Rabinowitch, of the Montreal General Hospital, made metabolic studies on a man, aged 47, suffering from diabetes insipidus with the following results. No single specific lesion was found to account for the polyuria. Functional analysis of the endocrine system showed hyperfunction of the pituitary body and hypofunction of the suprarenals. A balance was struck between these two abnormal functions, as was shown by the normal basal metabolism. The kidney function was normal in every respect except in its ability to concentrate salt. The hyperchloraemia found was apparently compensatory, aiding the excretion of salt, and was not a true retention since there was no clinical evidence of salt retention. The administration of pituitary extract definitely caused a diminution of the polyuria and an increased rate of flow with increased concentration of salt in the urine. Rabinowitch concludes that the theory that diabetes insipidus is produced by a lack of some internal secretion which normally regulates diuresis by acting on the renal cells is true in this case.

Symptomatology. Reverchon, Worms, and Rouquier report a fatal case of fracture of the base complicated not only by paralysis of several cranial nerves (V, VI, and VII), but also by diabetes insipidus (polydipsia and polyuria), intense anaemia and asthenia, low blood-pressure, puerilism, and apathy. The autopsy showed that the condition was due to severe lesions of the hypophysis, which was reduced to a small fibrous nodule in which no trace of normal tissue could be found on histological examination. The case suggests that the hypophysis is injured more frequently than is supposed in fractures of the base, either directly or indirectly, by compression by haemorrhage. The writers recommend that in fractures of the base one should look for evidence of diabetes insipidus as well as for the well-known signs accompanying this accident. X-rays will be of value in showing lesions of the posterior wall of the sella turcica.

Silvestri records the case of a man, aged 24, who developed diabetes insipidus at the age of 3 years after a severe intestinal toxi-infection. An arrest of mental and physical development took place, and it was not until the age of 20, when delayed puberty appeared, that the disturbed hormonic equilibrium was restored, as manifested by disappearance of diabetes insipidus and a normal skeletal development.

Evans and Wallis record two cases of diabetes insipidus complicated by glycosuria, the intermittent nature of which distinguished them from the cases of diabetes innocens described by Salomon (vide *Medical Science*, 1920, **2**, 313). The writers regard the cases as examples of a pituitary dystrophy comparable to those cases of thyroid dystrophy in which there is no marked change in the size of the gland and no distinct clinical picture of either hypo- or hyper-function.

Bergé and Schulmann summarize the characteristics of the polyuria in diabetes insipidus as follows: (1) The quantity eliminated is variable, no approximate figure being assignable. (2) The polyuria is more pronounced at night. (3) The quantity of urine excreted is at times greater than that of the fluid ingested (dehydration). (4) There are no notable modifications of the excretion attributable to variations of régime. (5) There is no important disturbance of the chemical composition of the urine. Generally speaking there is a slowing of metabolism and a tendency to demineralization. The amount of uric acid is small. There is no glycuronic disturbance. (6) Absolute renal integrity has been verified by (*a*) elimination of methylene blue, (*b*) persistence of the faculty of ureal concentration and maintenance of normal quantity. (7) Controlling action of extract of the posterior lobe of the hypophysis on the polyuria.

According to Antonelli, who records an illustrative case, Strauss in 1912 was the first to draw attention to the relation between diabetes insipidus and arrest of development, and cases of this kind have since been reported by Ebstein, Kopczynski, Lereboullet, Faure-Beaulieu and Vaucher, and Souques and Chauvet. In Antonelli's case, which occurred in a man aged 23, in whom arrest of development occurred at 13, pituitary involvement was shown by intense polyuria, attacks of headache and giddiness, asthenia, optic atrophy, bitemporal hemianopsia, low blood-pressure, and somnolence. In the absence of an autopsy the nature of the pituitary lesion could not be determined, but in view of the long history it was probably a benign tumour.

Gayler, of the Tübingen Children's Clinic and Institute for Physiological Chemistry, records a case of diabetes insipidus, in a girl aged 12, which had developed after an attack of pertussis at the age of 3. The amount of drink taken amounted to 5 litres a day. The case was remarkable for the great deficiency of growth which has been noted in many other instances of diabetes insipidus. Investigations were made into the metabolism of another case in which the diabetes insipidus was of recent origin and the daily amount of drink taken was between 5 and 6 litres. It was found that, owing to the large quantity of fluid consumed, a very considerable discharge of nitrogen and an increased excretion of lime took place, so that the loss of these substances, caused by the irrigation of the body with large quantities of fluid, could be regarded as the cause of the retardation of growth. Gayler does not suggest that this mechanical origin accounts for every case of infantilism connected with diabetes insipidus, since in the presence of other signs of endocrine disturbance it is obvious that insufficiency of the ductless glands is responsible. When, however, there is a retardation of growth only it may be justly attributed to the effect on metabolism of irrigating the growing body of the child with large quantities of fluid.

Christian, of Boston, records the case of a girl, aged 5, who presented the symptom-complex of diabetes insipidus associated with very extensive defects in the skull-bones and bilateral exophthalmus. Pituitary extract controlled the polyuria when given subcutaneously, but no other method of introducing pituitary substance had any effect upon the polyuria, and no method of giving pituitary substance had any influence on the bone defects or the exophthalmos. Only two similar cases have been recorded, viz., by Schüller, of Vienna, who, in a subsequent paper in which he comments on Christian's cases, comes to the conclusion that the syndrome is due to disease of the hypophysis, like acromegaly, dystrophia adiposo-genitalis, and pituitary dwarfism.

An example of the close functional and pathological relationship existing between the hypophysis and the thyroid is given by Ledoux, who reports a case of compression of the cavernous sinus associated with diabetes insipidus and conversion of a simple goitre into Graves's disease. The responsible lesion was probably situated in the hypophysis, the posterior lobe of which compressed the sinus and the nerves traversing it. The polyuria was of pituitary nature and was distinctly modified by an injection of extract of the posterior lobe. The nature of the pituitary lesion could not be determined, but it was probably not a gumma or a tumour, as the patient recovered without treatment.

Gorke and Deloch, of the Breslau University Medical Clinic, report three cases of diabetes insipidus in which, in addition to polyuria, polydipsia, anhydrosis, and increase in molecular concentration of the blood, the following gastro-intestinal symptoms were found: viz. hyperacidity, hypersecretion, increased gastric peristalsis and spastic constipation of the large intestine. The writers regard these disturbances of gastro-intestinal function as connected with the lability of the vegetative nervous system present in these cases, and attribute the favourable effect of pituglandol on the symptoms either to its direct action or to indirect action by the agency of the vegetative nervous system.

Prognosis. According to Schulmann and Desoutter the course and prognosis depend on the cause. Thus there is a considerable difference in the gravity of diabetes insipidus due to a malignant tumour and that due to pregnancy. Some cases are compatible with excellent health. The polyuria of syphilis may be considerably improved by treatment and sometimes even cured. The transformation of diabetes insipidus into diabetes mellitus has been recorded (vide *Medical Science*, 1919, **1**, 282).

Treatment. Schulmann and Desoutter remark that whatever its mode of action may be, extract of the posterior lobe of the hypophysis is the remedy of choice in diabetes insipidus. The best effect is obtained by subcutaneous injection. Although as a rule this treatment is unable to produce a disappearance of the causal lesion, it relieves for a time and in a striking degree the principal symptoms accompanying polyuria, especially the distressing thirst and vague discomfort which is the cause of insomnia. The treatment is perfectly harmless, and can be continued for a very long time without any bad effects. Examples of the success of subcutaneous injection are reported by Crouzon and Bouttier, Davidson, Flandin, Hubert, and Debray, Foerster, Gibson and Martin, Nasso, and Poulton. No appreciable effect was obtained when pituitary extract was given by mouth. (Davidson, Schnabel, and Gerhard.)

Cammidge reports a case of complete recovery from diabetes insipidus following lumbar puncture when about 1 oz. of cerebrospinal fluid in all was withdrawn under pressure. It is probable that the patient's symptoms were the result of parasyphilitic changes at the base of the brain which interfered with the passage of the secretion of the hypophysis into the cerebrospinal fluid. Withdrawal of some of the fluid owing to the sudden change of pressure within the spinal canal probably broke down adhesions and opened a channel for its normal passage again.

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THE NATURE OF ANTIGENS

Recent work by Carl C. Warden at the University of Michigan and at St. Joseph's of Mercy Hospital, Ann Arbor, has brought the question of the constitution of such compounds as the syphilitic antigen, various toxins such as those of diphtheria and anthrax, and even the yeast ferment, under one very comprehensive view-point. When it is said that the author seems to anticipate experiments on the nature of the cancerous process it will be seen that the scheme is a very wide one indeed.

For a long time attempts have been made to arrive at the composition of toxins, and the problem has proved to be one of extraordinary elusiveness. Originally there seemed to be no doubt that they were of protein origin—possibly compounds like albumoses, peptones, or ptomaines. The thing which has struck many investigators is the fact that if attempts were made to obtain them in a greater state of purity, the characteristic tests for protein became less marked. Jacoby (1) in purifying ricin got a compound which had all the characteristic features of the toxin, but was destitute of protein reaction. This has been confirmed with other toxins. Some experiments are recorded, such as those of Belfanti, in which purification of a toxin led eventually to a nucleo-proteid. Even antitoxins have been scrutinized as to their protein character, for both Pröscher and Jacoby (2) have obtained antitoxins which gave no protein reaction. There has always been, of course, the possibility that the non-protein substances eventually found were in reality contaminated with an exceedingly minute quantity of a most potent compound which eluded even delicate chemical tests.

All this was quite apart from a closely-related question as to whether the toxins were metabolic excreta of the bacteria, results of the disintegration of dying or dead cells, or whether they were synthetic products of the medium elaborated by the action of the bacteria. For this last point of view there is the well-known fact that certain media allow of vigorous growth without the production of toxin, and that other media in which growth is no more luxuriant produce potent toxin.

At the present moment the trend of biological study is towards colloid chemistry, and it is certain that in many departments we have enlarged our knowledge of vital processes by taking into consideration the surface properties of protoplasm, and all that this implies. Instead of viewing a cell as a unit having a surface roughly corresponding to a sphere of the same size, we now look upon it as an aggregation of particles, the surfaces of which may be many times that of the original cell, and as reactions are known to take place at the surfaces (interfaces) a greater opportunity is presented for these reactions to occur.

One other recent development in this connexion is of importance. The beautiful experiments of Irving Langmuir have shown that on the surface of water one may have fatty acids distributed in a layer, one molecule deep, and, what is of even greater interest, these molecules are packed in a perfectly orderly fashion with the $-COOH$ group attached to the water and the long hydrocarbon chain standing up perpendicularly, as it were, out of the water surface. It has been estimated that the molecules contained in 2 mgm. of fatty acid such as stearic acid are sufficient in number to cover completely a surface of water ten square metres in area with a layer of the acid molecules one molecule in depth. One can see, therefore, what a powerful effect might be exerted on a suitable surface by a minute quantity of a fatty acid.

With this very fragmentary preliminary we come to the idea underlying Warden's work. He assumes, and attempts to prove, that toxins, haemolysins, the syphilitic antigen, and even the zymase of yeast, which transforms glucose to carbon dioxide and alcohol, are arrangements of fatty acids dispersed on the surfaces of protein or other suitable aggregates. Toxins and haemolysins are merely different phases of the degree of dispersion of the fatty acids employed.

He believes 'that the specific antigens of cells, bacterial and somatic, consist of the various fatty complexes which are peculiar to the different species of cells, and which bestow upon their particulate surfaces definite chemical character'.

It will be seen from this that the specificity of a toxin will be dependent on (1) the composition of the fatty acids which are to be dispersed in some surface, and (2) the type of surfaces which receive them. That there is ample room for all the countless antigens which exist is possible if one concedes that the fatty acids may form—so to speak—mosaic patterns on the surface on which they are dispersed, and so one may visualize a very perfect mechanism for the lock and key effect which one so often thinks of in the combination of toxin with cell receptor.

Warden's work started with an investigation of the mechanism of the vaccine treatment of gonorrhoea (1 and 2). In these papers he showed that the fatty acids obtained from the cocci could be used for complement fixation tests in the same way as could the organisms themselves. Further, clinical treatment, using all the fats distributed on an oil-water emulsion as a vaccine, gave curative results equal to or even better than those obtained by the injection of gonococcus vaccine itself. In a discussion of his results which took place at the meeting of the genito-urinary section of the American Medical Association in June 1916, it appeared that clinicians who had used this type of vaccine were very favourably impressed with its efficiency. According to the reports of its use it was much more constant in its effects than the ordinary gonococcal vaccine.

In complement-fixation tests the fats behaved in a manner similar to gonococcus antigen. From this he and Kelly were led to investigate the nature of syphilitic antigen, and in this they traverse ground which has been worked over by other investigators. We already know that a variety of substances may function in the Wassermann test in deviating complement, and that it is not necessary to have a specific antigen for the purpose. There is, however, a considerable difference in the usefulness of the various 'lipoid' substances which are used for the purpose. For example, the 'lipoids' from human hearts are more efficient than those from other animals.

Warden and Kelly were led to examine the lecithins from human hearts, and determined that they consisted of approximately capric acid 10, palmitic acid 40, stearic acid 5, oleic acid 30, linoleic acid 10, and clupandonic acid 5, combined with glycerophosphoric acid, choline, and probably other bases. It was shown that the purified lecithin was equal to, if not superior to, the best crude alcoholic extract commonly employed as antigen. The word 'antigen' in this connexion they believe to be a misnomer. Antigens act rather by virtue of their power of lowering surface energy between the colloid systems in the serum so as to produce aggregation and absorption of complement.

In the next paper Warden (3) takes up the rôle of specific fats in complement fixation. For this purpose mass cultures of the organisms of cholera, typhoid, and tuberculosis were made. The bacterial mass was saponified with sodium alcoholate under 100° C., and after liberating the fatty acids these were converted into the sodium salts. These salts gave specific complement fixation, using amounts of about 0·002 gm of the sodium salts. In the case of tuberculosis the test failed owing to the absence of sensitizers in the sera, but in all the others the tests were comparable with those obtained with a normal antigen. In addition, he was able to prepare from sheep's corpuscles antigen in the form of sodium salts of the fatty acids, which when incubated with sensitizer and complement absorbed the latter.

In the following paper he (4) investigates the types of colloidal particles on which the fatty acids are dispersed, using the specific fats of red blood cells. The two surfaces employed were an aqueous suspension of typhoid bacilli which had been killed, fixed with 1·0 per cent. formalin, washed, and kept in distilled water for a year. This suspension gave no protein reaction. An aqueous colloidal suspension of protein-free cholesterin was also used. On these colloids the fatty acid salts from blood corpuscles were dispersed. Rabbits were then immunized with the mixture. Immune reactions were then performed with the sera of the immune animals, and in all but one case an immune body to red cells of the sheep were obtained on test. What were even more striking were the results which he obtained by the analysis of the fats isolated from a large quantity of sheep's red cells. In a tentative way he came to the conclusion that the fats were in great part a mixture of certain fatty acids, melissic, cerotic, and clupandonic. The sodium salts of a mixture of the pure acids were injected into animals after being dispersed on typhoid cells and are cholesterol. These also gave positive immunity tests against red cells.

The tests with gonococcus and typhoid antigens were repeated, and the work extended to embrace the pneumococcus (4). In all cases the results were positive in showing that immune bodies were produced in the animal following the injection of suitably dispersed fatty acid salts. Precipitation tests also confirmed this. In the discussion in this paper Warden goes more fully into the relative importance of proteins and fats in immunity processes and attempts to show that, in the great importance which has been assigned to the former, the place of fats has been disregarded. He points out that while in the case of egg white, the antibody against egg white will react to all white of egg from whatever species of bird it is obtained, the fat immunity-process is one of a much greater specificity. The group relationships in such organisms as the pneumococci and typhoid bacilli are characterized by minute variation of the same fatty constituents. Dissimilar organisms such as the gonococcus and the tubercle bacilli have fats wholly dissimilar.

In his next paper (5) he deals with the pneumococcus, an organism which is known to form an antibody of high specificity but of low protective power. Here he takes into account the differences which are encountered between true protein antibody production, which is characterized by the large amount produced but limited specificity, and the antibody production to fatty acids, which is so highly specific. The possibility arises that in the immunity behaviour of the pneumococcus the faulty production of large amounts of immune bodies may lie in the type of protein on which the fatty acids are dispersed. This appeared to be incorrect, but the protective power of the antibody did increase if suitable dispersion of the acids was obtained. In this instance cholesterin afforded a suitable base, although the improvement was not marked. He notes, however, that, in the varying composition of the fatty acids obtained from bacteria, those organisms which furnish enduring and protective antibodies (typhoid) contain fatty acids from the middle of the fatty acid series. Those which contain fatty acids of the lower and upper members of the series are less prone to form good protective sera. To this latter class the pneumococcus belongs. He concludes this paper with an earnest suggestion that, when the methods of dispersion are worked out, on account of their purity, the possibility of accurate dosage, and the absence of toxicity, the fatty acid antigens should recommend themselves for protective inoculation.

The succeeding paper (Warden and Connell) on the antigen of *B. anthracis* is one of almost dramatic interest. From mass cultures of this organism he was able to get such large quantities of the fat as to be able to make a tentative analysis. The fat contained caprylic acid, capric, oleic and palmitic acids. About half of the mixture was thought to be oleic acid. With trial mixtures he ascertained that a mixture containing caprylic 10 per cent., capric 25 per cent., oleic 60 per cent., palmitic 5 per cent., gave immunity reaction most closely simulating the natural fatty acids from the bacteria.

It was found, moreover, that the fatty acids as mixed above were able to prevent the growth of the bacilli from spores in quantities at 0·0006 mgm. in 10 c.cm. of medium. A more extraordinary phenomenon however follows. An attempt was made to use the fatty acid antigen to produce a protective serum in guinea-pigs. Half a milligramme was injected daily for three days. These animals died of anthrax. The most complete controls were made, concerning which it is impossible to enter here. The explanation of this most remarkable occurrence was that the hay on which these animals were fed contained anthrax spores. The animals passed through a negative phase, which allowed auto-infection to take place. On the other hand, by suitably dosing protective amounts of the artificial antigen in rabbits, he was able to make them withstand ten times the lethal dose of the bacteria, but not a hundredfold dose. In no case was the protein of anthrax necessary for the mechanism of the immunity.

There now follow two papers (Connell and Holly, and Warden, Connell, and Holly) on the nature of haemolysins and toxins, which will be considered together.

In the consideration of haemolysins, streptococcus, which had been previously investigated by Warden, and *B. megatherium* were employed. The fatty acid salt antigens were dispersed in broth, and this broth used for haemolysis. The amounts used in the broth varied between 32 and 120 mgm. per litre. Haemolysins prepared in this way were not as active as the natural products. This was explained by the slow and more efficient manner in which the bacteria liberate their fatty acids into the medium, with probably emulsifying substances at the same time. This is difficult to imitate where one has a solution of the salts in alcohol which must be added to the broth which is to form the eventual solution of lysin. Certain very suggestive points are brought up. One is that the colour of the broth has an effect on the potency of the lysin produced, and the other is that filtration of the broth through a Berkefeld filter impairs its capacity for forming lysin. In the latter case the filter has taken out colloidal particles of the proper character for dispersion, and in the former the colour denotes the presence of particles, e. g. humin substances, suitable for receiving the fats. In the case of *B. megatherium* the artificial lysin gave rise to a strong antilysin.

In the paper on toxin much interesting ground is covered on the toxins of *B. diphtheriae* and *B. megatherium*, but what strikes the reviewer as most important are the experiments showing the influence of proper dispersion on the potency of the artificial toxin. Numbers of media were tried on which the salts were dispersed. That which gave the most powerful toxin was prepared by adding the alcoholic antigen to a dilute solution of haemoglobin. When this was added to a standard broth a clear solution was obtained, even when the amount of fat antigen exceeded 200 mgm. per litre. This artificial toxin in one instance killed a guinea-pig on the first day with typical lesions of diphtheria. The discussion in this paper is interesting, for Warden and his co-workers attempt to analyse the mechanism of antigens which produce a good or a poor response. In the case of *B. diphtheriae* the definite size of the antigen particle may be the determining factor. *B. megatherium*, on the other hand, will yield all antibodies even if the size of the particles be variable. Streptococcus gives poor antibodies either with the bodies of the organisms or with the artificial antigen.

The principal conclusion in these two papers is stated in the words of the authors: 'All antigen-antibody reactions, from agglutination and precipitation through complement fixation to toxin-antitoxin aggregates, are but phases of the same phenomenon acting from one extreme of the colloidal realm to the other, and that all phases must be possible with all antigens, if only the proper colloidal state can be found.' Hence the lysins and toxins of *B. diphtheriae* and *B. megatherium* are the same substances—the specific fat antigens of the micro-organisms existing in definite and particular colloidal states. Aside from colloidal or emulsifying activity, cellular protein appears to have no place in the immune reactions studied.

The last paper, which only appeared in October, is of great interest to biochemists, because it brings a ferment, the zymase of yeast, into the category. By dispersing sodium oleate on fibrin, earthenware, pumice, or sponge, he was able to ferment glucose to alcohol and carbon dioxide. If these experiments are capable of easy repetition, they will go far to revolutionize our views as to the general nature of ferments.

The work of Warden and his colleagues has been given without any attempt at criticism on the part of the reviewer. It is felt that the subject is too important to comment upon without a certain amount of knowledge based on repeating the experiments. Certain of the experiments as given are not altogether satisfactory from the immunologist's point of view, but it must be borne in mind, as Warden himself points out, that the composition of the fatty antigens employed are not exactly known, and more especially the difficulties of dispersing them in a way which will imitate the natural products are great. For this reason the artificial antigens cannot as yet compete in point of specificity or potency with the natural products.

The work is obviously that of a competent and thoughtful experimenter, and confirmation of it by others will be looked forward to by all who are interested in problems of immunity. Should this confirmation be forthcoming, the views which Warden has expressed would clear away many of the difficulties with which the modern conceptions of immune processes are beset.

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Jacoby, M. (1). Über die chemische Natur des Ricins. *Arch. f. exper. Path. u. Pharmakol.*, 1901, **46**, 28.

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ERRATUM

Volume V, Number 5, page 407, line 10, for *J. Am. M. Ass.* read *Tr. Sect. Path. & Physiol. Am. M. Ass.*

Medical Science April

Warden, C. C. (4). Specific fats as factors in immune processes. *J. Infect. Dis.*, 1918, **23**, 504.

Warden, C. C. (5). The function of fats in immune processes. II. *Pneumococcus* and *Streptococcus* immunity. *J. Infect. Dis.*, 1919, **24**, 285.

Warden, C. C. (6). The nature of alcoholic fermentation. *Am. J. Physiol.*, 1921, **57**, 454.

Warden, C. C., and **Connell, J. T.** The antigen of *Bacillus anthracis*. *J. Infect. Dis.*, 1919, **25**, 399.

Warden, C. C., and **Kelly, J. B.** The nature of the syphilitic antigen. *J. Am. M. Ass.*, 1917, 96.

Warden, C. C., Connell, J. T., and **Holly, L. E.** The nature of toxin. The antigen of *Corynebacterium diphtheriae* and *Bacillus megatherium* and their relation to toxin. *J. Bact.*, 1921, **6**, 103.

C. G. L. W.

ABSTRACTS

SURGERY

Delannoy, E. Fractures de la cavité cotyloïde par enfoncement et luxation centrale du fémur. [**Fractures of the acetabulum by driving inwards of the femur and central dislocation of the hip-joint.**] *Rev. de chir.*, 1921, **59**, 317.

This article refers to isolated fractures of the pit of the acetabulum and excludes the fractures of the pelvis which cross the acetabulum while involving other parts of the bone, and also the fractures of the rim of the acetabulum which are associated with many posterior dislocations of the hip. The fractures under discussion are almost always produced by the same mechanism, the driving inwards of the head of the femur. Thus the fractures and the central dislocation of the femur are degrees of the same injury and should not be considered separately. The author regards the condition as important because it leads to frequent mistakes in diagnosis and to serious medico-legal consequences. He has had experience of one case and has references to fifty-three others occurring since 1904. His own case was that of a bricklayer who fell on to his right hip. He had a moderately severe pain in the region of the right great trochanter. There was no bruising but Scarpa's triangle was swollen and the line of the groin had disappeared. Above Poupart's ligament was a line of induration passing up to the anterior superior spine. The only tenderness found was that elicited on forcible percussion of the great trochanter. The trochanter was not raised. There was slight external rotation of the thigh, which could be easily corrected, and the movements of the hip-joint were practically normal and painless except that extreme flexion caused pain. The limb was shortened by ½ cm. The patient could stand without support, and could stand on the injured leg if supported by the opposite hand. X-ray showed a fracture of the acetabulum, the femur having been driven into its cavity and the contour of the true pelvis showing distortion. On rectal examination, a soft swelling of the right half of the pelvis was found, pitting on pressure and tender. In two days the swelling of Scarpa's triangle had increased and a large haematoma developed. There was no alteration in the signs felt per rectum. Patient was discharged 5½ weeks after the injury, when the shortening was the same, but there was limitation of all movements of the hip. He was seen again a fortnight afterwards, when the shortening had increased to 1 cm., and the ankylosis of the hip was complete. He walked with pain and with a well-marked limp. A radiogram showed that the head had penetrated about 1 cm. more deeply into the acetabular cavity, and that there was a definite line indicating the formation of a new joint. There was also new bone around the cotyloid notch.

After an historical account of recognition of this injury, its aetiology is discussed. In 48 cases 16 recurred between 30 and 40 years of age, and in 53 cases 12 were women. All cases except one gunshot wound were due to indirect violence, the character of which showed the following order of frequency: falls on to the great trochanter, falls on to the feet, and, least common, severe blows on the shoulder.

Experimental attempts to confirm the apparent mechanism by which falls on to the great trochanter produce this lesion were not immediately successful. (This work was done by other surgeons.)

A blow on the great trochanter of a corpse usually causes fracture of the neck of the femur, and only rarely produces the injury under consideration, but by substituting a boxwood femur they found it possible to reproduce the acetabular fracture with penetration by the head. The author therefore considers that a resistant neck is necessary, and quotes a case with autopsy where a dense eburnated neck was found. The resistance of the acetabulum is another factor, and destruction by hip disease is considered a predisposing cause. Resistance of the acetabulum is slight compared with that of the femur, but it is increased by the ligamentum teres which forms a thick cushion filling the deep posterior part, the thinnest portion, of the acetabulum. This ligament has been removed by Tillaux in order to produce the injury experimentally. The author considers that the direction of the violence is of importance, and points out that less resistance by the acetabulum will be met with if the violence be transmitted to the thinnest part, that is, the posterior inferior part, of the bottom of the cavity. This appears more clearly in the mechanism in falls on the feet. In this case the fracture has not been reproduced experimentally except when the hip is widely abducted. In the erect position the force of a fall on to the feet is transmitted to the edge of the acetabulum and an iliac dislocation results. Blows on the shoulder produce the injury by transmitting the force through the vertebral column and the pelvis, which impales itself on the head of the femur.

With regard to the inward dislocation of the femur, this is due either to the original violence or to secondary trauma, as by walking or by muscular action. The latter has been observed in radiograms taken at intervals after an accident in which there was no immediate penetration by the head.

The morbid anatomy of these fractures shows that they tend to follow the lines of junction of the three bones of the acetabulum, although the suture lines have disappeared. They are of three types: vertical, horizontal, and stellate, the latter being associated with pelvic penetration by the head of the femur. Occasionally there is a fracture which passes round the margin of the acetabulum causing detachment of a central fragment which enters the pelvis with the femoral head. Sometimes the fractures radiate from the acetabulum to all parts of the pelvis.

In the displacement there are three degrees. First, simple fragmentation of the acetabulum. Here there is no displacement as the fragments are held together to some extent by the musculature of the wall of the true pelvis, and by the periosteum, but mostly by the interlocking of the fr ments. These cases are usually diagnosed as contusions. The second de is that in which there is some penetration of the head of the femur apices of the acetabular fragments entering the pelvis, their bases rema attached to the cotyloid rim. The third degree is that in which the fe is dislocated inwards, the head passing entirely within the pelvis. In such cases the dislocation of the head is arrested by the great trochanter when the latter meets the cotyloid rim. These degrees are somewhat theoretical, as the extent of the penetration of the head of the femur does not necessarily correspond exactly with the degree of fragmentation of the acetabulum.

It is possible for the head to enter the pelvis completely, and at the same time it may be impossible to reduce the dislocation by any external manipulation, because the head may be wedged in its new position by the acetabular fragments. Further, the fragments need not follow precisely the path of the head, as in a case in which a fragment was found at operation wedged between the femur and the remains of the acetabulum.

The capsule of the hip-joint and the round ligament are often torn, as also are the obturator internus and the psoas muscles. A haematoma frequently occurs, and there is a tendency to suppuration in it. Lesions of vessels, nerves, and viscera may also complicate the lesion.

Symptoms. Functional impairment is not usually absolute. The patient can in some cases take a few steps. Pain varies; sometimes it radiates from the hip to the thigh and abdomen, and may be so severe that examination may prove impossible without an anaesthetic; in other cases the patient hardly suffers at all. Not much diagnostic importance can be attached to the pain, except that severe pain in the inner aspect of the thigh may point to a lesion of the obturator nerve. Visceral complications may occur.

Physical signs. Attitude of the limb: slight flexion, external rotation, and abduction are common, but flexion, internal rotation, and adduction may occur. These variations depend on the character of the destruction of the capsule and musculature. Disappearance of the prominence of the trochanter may be masked by swelling. Ecchymoses occur particularly near the trochanter, in the groin, and in the scrotum. The appearance of the last two may be delayed for a few days. There is soft swelling above Poupart's ligament corresponding to the haematoma in the pelvis. Occasionally the head may be felt inside the pelvis. The effusion over the hip-joint is felt in Scarpa's triangle. The trochanter is raised and percussion over it is painful.

The only movement constantly limited is abduction, its diminution being due to the great trochanter meeting the cotyloid rim. If there be no limitation of movement a diagnosis of contusion may be made, although there may be a fracture of the acetabulum without displacement.

Measurement may show shortening which is an index of the degree of penetration of the head into the pelvis. Shortening may be primary or may occur secondarily during the months that elapse after the injury. Shortening of the lines from the trochanter to the anterior superior spine and to the pubic spine indicates the degree of penetration of the head, and in addition the great trochanter may lie internal to a sagittal line through the anterior superior spine instead of external to it as is normal.

Rectal or vaginal examination discovers a swelling which may be firm soft (haematoma), or may be hard, globular, and moving with the thigh ocated head of the femur). Crepitus may be felt. Or, if there be no acement of the head, a very tender spot may be found in the pelvic wall.

The diagnosis must be made between contusion of the thigh (most non mistake), fracture of the neck of the femur, and all the dislocations of the hip. Obturator dislocation where the head has passed through the obturator membrane into the cavity of the pelvis has been observed. If the case be seen after the lapse of some days, disease of the hip or tumour of the pelvis may be wrongly diagnosed. A good radiogram and rectal examination are important.

Complications. The obturator, gluteal, and external iliac vessels have been injured. Thrombosis of the internal iliac vein has occurred from compression by the haematoma. Nerve lesions are rarely severe and may be complete or incomplete. They most commonly occur as a result of inclusion of the nerve in callus. The obturator nerve is that most commonly injured. It causes severe intractable persistent pain. Intraperitoneal lesions are rare, but a peritoneal reaction is commonly manifested by vomiting, meteorism, and abdominal pain and rigidity. This may de due to puncture of the peritoneum by a fragment of bone, but is more commonly reflex and initiated by a subserous effusion of blood. Laparotomy, especially if done under local analgesia, will not prejudice the prognosis gravely, will settle such questions, and will make possible treatment of the associated injuries. Retention of urine is very common and is most often reflex, but may be due to injury to the pelvic nerves by a haematoma. Rupture of the bladder is rare and only likely to occur when the viscus is distended. Incomplete rupture with haematuria but without escape of urine may occur. Rupture of the urethra is sometimes found. Rupture of the intestine is very rare. Obstetrical difficulties may occur later.

Course and prognosis. The mortality is not so great as has been supposed. The author gives three deaths in 53 cases. A considerable portion of the deaths is due to septicaemia following suppuration of a pelvic haematoma. The prognosis as regards function is still bad, ankylosis of the hip and 2 to 5 cm. of shortening being common. Radiography shows the formation of a new joint between the head of the femur and the fragments of the acetabulum, and the development of bony outgrowths from the acetabular rim. It is probably the latter, together with the progressive yielding of the new acetabulum, that causes the limitation of movement.

Treatment of the fracture. When there is little penetration of the head, treatment by extension and movements can be adopted. The danger in such cases is the onset of traumatic arthritis. When there is inward dislocation of the head, reduction may be effected by manipulations alone, or by open operation. Where the acetabulum alone is fractured, wide and complete abduction of both limbs, with extensions of the injured one, as advised by Whitman, will reduce the dislocation. Abduction is to be maintained in plaster for several months. The authors do not recommend replacement of the head in the acetabulum with the finger in the rectum because of the danger of damaging the latter. If the pelvis be fractured as well, gradual and progressive extension in a lateral direction as well as in the long axis of the thigh will sometimes succeed in reducing the displacement. Open operation is reserved for the cases where the other manœuvres fail. Immediate operation has most often been done for visceral complications, the dislocation having been left alone. Open operation in cases where the dislocation cannot be reduced has been performed through several incisions. Kocher's incision for exploration of the hip is not suitable because the great trochanter is pressed up against the upper lip of the acetabulum. The anterior route to the hip-joint gives better access. An incision as for exposure of the external iliac artery gives access to the head dislocated into the pelvis. Through this incision the pelvic haematoma should be cleared out. In all cases movement should be undertaken towards the third or fourth week, and a suitable apparatus should be worn when the patient gets up.

Treatment of complications. Abdominal injuries should be dealt with. Suppuration of a haematoma should be treated by wide clearance and drainage. This is a serious complication. In old cases operation may be necessary for malposition or for nerve pains. For the former, forcible breaking down of an ankylosis or sub-trochanteric osteotomy with the establishment of the proper degree of abduction may be performed. For the latter it may be necessary to free the obturator nerve from callus. This may be done through an incision as for exposure of the external iliac artery by the extraperitoneal route. J. T.

Roch, G. Über die Rolle der Erblichkeit in der Ätiologie der Luxatio coxae congenita. [**On the part taken by heredity in the aetiology of congenital dislocation of the hip.**] *Zentralbl. f. Chir.*, 1921, **48**, 1314.

The author has had an opportunity of investigating 189 cases of congenital dislocation of the hip in the clinics of Professors Perthes and Heineke. This disease in ten years had an incidence of 0·28 per cent. among the 67,429 cases of all sorts, in the clinics. 15 per cent. of the patients were males and 85 per cent. females. The author gives a summary of 115 complete family trees which formed the foundation of his research. He says that this condition is a hereditary stigma whose occurrence is associated with several factors. His inquiry has led him to the following conclusions:

Congenital dislocation of the hip is either dependent upon a combination of factors, or an inherent tendency, in the embryo. Various accidental conditions, intra-uterine injuries, or injuries from outside causes, are observed as causes. A summary of the family histories is attached, representing 1,272 individuals, of whom 152 had congenital dislocation of the hip. Of the total number 57 were afflicted with alcoholism, epilepsy, or insanity. Roch is of the opinion that the condition is a sign of a familial degeneration or decay. 34 of his family trees can be taken as evidence for such a belief. One tree shows, in four generations, five cases of congenital dislocation of the hip, two examples of insanity, one case of internal hydrocephalus, several cases of early death, and one case of death of the mother during childbirth. J. T.

Allison, N., and **Brooks, B.** **Bone atrophy. An experimental and clinical study of the changes which result in bone from non-use.** *Surg. Gynec. & Obst.*, 1921, **33**, 250.

Dogs were used in these experiments. In each case use of one foreleg was prevented. Methods used were: section of the brachial plexus; excision of the upper end of the humerus; plaster of Paris fixation. X-ray plates, morbid anatomy and histology, chemical composition, breaking strength, growth and regeneration were examined. The following results appeared from these experiments: No matter how the disuse was caused the bone changes were the same, and appeared rapidly in the bone within a week. There was no chemical change in the bone. In the case of a growing bone disuse retarded but did not stop growth; the retardation occurred more in the shaft than in the epiphysis, as shown by the relatively narrow shaft and wide epiphysis. In adult bone disuse caused no change in length but a slight diminution in diameter. There was considerable decrease in the cancellous tissue and the medullary cavity was increased in diameter. The periosteum became unnaturally adherent to the shaft. The breaking strain was diminished only in proportion to the amount of diminution of bone in the shaft. With transplants of bone from and to used and disused bone no variation in the amount of bone produced could be observed. Bone atrophy is not a change in the characteristics of bone but in the amount of bone present. J. T.

Jacobaeus, H. C. About the cauterization of adhesions in pneumothorax treatment of tuberculosis. *Acta Chir. Scand.*, 1921, **53,** 293–338.

Christoffersen, N. R. Afbrænding af Pleuraadhærencer efter Prof. Jacobæus' Metode. [**Cauterization of pleural adhesions by Professor Jacobaeus's method.**] *Ugesk. f. Læger.*, 1921, **83,** 243–9.

Jacobaeus prefaces his account of cauterization of pleural adhesions with a reference to the fact that, in the pneumothorax treatment of pulmonary tuberculosis, these adhesions often prevent this procedure being effective. He describes in detail the technique he has evolved, and gives a full account of his cases, which now amount to 40. His discussion also refers to other publications and to cases not yet published by other workers, and he calculates that, altogether, this operation has already been undertaken in about 100 cases.

Of the complications, haemorrhage is one of the most serious, and several operators have encountered it. But only in 6 out of about 100 cases was there any appreciable haemorrhage, and none terminated fatally. The most severe haemorrhage was observed by Dahlstedt, whose patient collapsed with a small, quick pulse. An attempt to close the vessel by renewed cauterization did not succeed, and the ultimate arrest of the haemorrhage occurred automatically without further interference. The risk of this complication can be greatly reduced by keeping the cautery at a dull red, not a white, glow. Should a haemorrhage occur in spite of this precaution, the intrapleural pressure should be raised by the injection of air or saline solution. Another possible remedy is to seal the bleeding-point with the cautery. A further complication is pleural effusion, but though this is common it is seldom permanently harmful. In 19 cases no effusion followed the cauterization, and in 12 others a small effusion disappeared in a week or two. In 3 cases there was a bulky effusion with fever; both vanished after several weeks. In 4 cases an effusion provoked by the cauterization turned into chronic empyema, and 3 of these cases terminated fatally within two years. In the fourth case the empyema persisted for more than a year, but the patient ultimately recovered. Altogether it would appear that a pleural effusion is provoked in about 50 per cent. of all cases and is of two varieties. The first is comparatively benign and is probably due simply to thermal irritation, disappearing in a week or two. The other is far more serious, is directly of tuberculous origin, and may terminate in chronic empyema and death. It seems to be an unavoidable complication, and is responsible for the 8 per cent. mortality rate of this operation. No case of air embolism has yet been recorded as a complication, but surgical emphysema is a comparatively common, but not a very serious, sequel to the operation.

In 30 out of the 40 cases severance of the adhesions led to the desired collapse of the lung. In 27 cases of apical or lateral adhesions, complete or 'sufficient' compression of the lung was effected. Several diaphragmatic adhesions were successfully severed, but only in one of these cases was the ultimate result satisfactory. In none of the 100 cases hitherto treated does cauterization of adhesions appear to have established a communication between the interior of the lung and the pleural cavity, giving rise to septic infection of the latter.

Christoffersen's records of 3 cases of artificial pneumothorax, in which plural adhesions were severed by cauterization, show that the operation can be practically painless when anaesthesia is induced with care and skill. In one of his cases a partial pneumothorax had effected some improvement, but complete recovery did not occur till, by cauterization of adhesions, an incomplete pneumothorax was made complete. The desired effect was not achieved in the other 2 cases. The operation requires considerable practice and technical finesse, but is comparatively easy when the operator has familiarized himself with its details. C. L.

Waters, B. H. Pleural infection complicating artificial pneumothorax treated with gentian violet. *Am. Rev. Tuberc.*, 1921, **4**, 875–81.

Encouraged by the accounts published by Churchman as to the effect of gentian violet on pathogenic organisms infecting joints, Waters has used it in two cases of septic infection of the pleura with marked success. In both these cases the pleural cavity became infected in the course of artificial compression of the lung for pulmonary tuberculosis. In the first case, *Staphylococcus aureus* and a diplococcus, resembling the pneumococcus, were found in the pleural effusion. The patient seemed moribund, her temperature being 105·6°, her pulse 160, and her respiration 52. After the pleural cavity had been washed out with saline solution, a 1 in 5,000 solution of gentian violet was introduced. Some of it was slowly withdrawn several minutes later, but about 150 c.cm. were left. The following morning the temperature fell by crisis, and there was marked improvement in the pulse and respiration. The treatment was repeated next day, and continued every other day until the secondary infection was under control. The strength of the solution was gradually raised to 1 in 2,500 without indications of pleural irritation or toxic effects. Within four weeks of the first irrigation smears and cultures were negative. The result in the second case was even more gratifying, and again the bacteriological reports coincided with the clinical observations. C. L.

Frischbier, G. Lungenschüsse und Lungentuberkulose. [**Gunshot wounds of the chest and pulmonary tuberculosis.**] *Ztschr. f. Tuberk.*, 1920, **33**, 7–8.

Seitler, O. Brustschüsse und Lungentuberkulose. [**Gunshot wounds of the chest and pulmonary tuberculosis.**] *Ztschr. f. Tuberk.*, 1920, **33**, 1–7.

Among 2,359 army patients in his chest hospital, Überruhr, in Würtemberg, Seitler found 33 with gunshot wounds of the chest. The interval between infliction of the wound and the onset of signs of active tuberculosis varied from four weeks to five years. In the case of soldiers who had previously shown signs of tuberculosis, this interval averaged five months, whereas it averaged 26 months in soldiers without a personal or family record of tuberculosis. In most cases the pulmonary disease appeared first, and was most severe, on the wounded side. Seitler concludes that reactivation of old tuberculous lesions in the lungs by gunshot wounds is not as rare as is commonly supposed.

Frischbier, of the Beelitz Chest Hospital in Germany, found that among more than 6,000 patients there were only 83 with gunshot wounds of the chest, and only 46 of these patients suffered from active pulmonary tuberculosis, the onset of which could be correlated with the wounds. While admitting that gunshot wounds may stir previously latent pulmonary tuberculosis into activity, he does not consider this sequence to be common.

C. L.

Donati, M. Decorticazione e pneumopessia nella cura operatoria dell' empiema cronico fistolizzato. [**Decortication and pneumopexy in the operative cure of chronic discharging empyema.**] *Arch. ital. di chir.*, 1921, **3**, 517.

The author records a case of some months' standing in which he operated successfully by a method elaborated from those of Estlander, Schede, Delorme, Rovsing, and others, and designed to obliterate dead space by bringing viscus to wall, rather than permitting wall, no longer rigid, to reach the surface of unexpanded and functionless lung. He employs the ordinary means to secure preliminary disinfection—opening up sinuses, drainage of recesses, Dakin irrigation, and so on. Exposure of the entire cavity is attained by an incision between 8th and 9th ribs, beginning at the angle, close to the spines, extending to the posterior axillary line and thence upwards and forwards across three or four ribs, which are divided in the same line. The flap thus marked out is raised as a whole, the ribs being fractured at or near their angles. Through this very large opening the process of decortication is carried out, beginning with the under aspect of the flap, continuing to the costo-vertebral angle at the reflexion, on to the visceral surface, denuding the lung from apex to diaphragm, and eventually removing the organized exudate mass as one piece. It is stated that if the right interval be found, the pleural surface may be left smooth and shining almost as normal, certainly over the lung, probably not intact except as to the elastic layer over the parietes, and generally only by scalpel dissection from the diaphragm. In the case recorded all this was possible, and the lung expanded forthwith so well as almost to impede by its exuberance the later stages of the decortication. The fixation was accomplished by multiple wide U-sutures of catgut grasping lung tissue and passing through the intercostal muscles to be tied on their outer aspect beneath the flap of skin and soft parts. With but minor troubles, the case recovered. There was hardly any deformity of the spine or thorax and there was also a fully-functioning lung. E. R. C.

Torraca, L. La plastica epiploica del mesenterio. [**Substitution of omentum for mesentery.**] *Policlin.*, 1921, Sez. chir., **28**, 332.

This paper describes experiments on dogs to discover what length of intestine, large and small, partly or completely isolated from its mesenteric blood-supply will live; and to what extent attachment of great omentum to the isolated loop aids in survival. Complete or partial isolation is to be interpreted as indicating section of the mesentery close to the bowel or attachment at such a distance that blood can reach part at least of the loop via the arcades. The omental graft may perhaps control the escape of contents from bowel which would otherwise have perforated before the re-establishment of circulation, but neither on large nor small bowel is the length of viable loop materially increased, and there is a definite danger of occlusion of the bowel by contraction and cicatrization. It appears, as might be expected, that the time permitted, before necrosis of the mid-loop, is not enough for vascularization of the bowel-wall from the mesenteric vessels. E. R. C.

Parlavecchio, G. (1). I. Diagnosi e cura delle affezioni gastroenteriche e nervose prodotte dalle ptosi viscerali. [**Diagnosis and treatment of the gastro-intestinal nervous disorder due to visceroptosis.**] *Arch. ital. di chir.*, 1921, **4**, 43.

Parlavecchio, G. (2). II. Le basi razionali della chirurgia ortotetica viscerale. [**The rational basis of corrective surgery of the viscera.**] *Arch. ital. di chir.*, 1921, **4**, 165.

These two papers review the subject pretty thoroughly, with a useful analysis of the natural means by which position is maintained, and suggest that the operative procedure of choice should reinforce 'suspension' by tissue grafts or other means in the case of organs primarily suspended; should under-sling those normally 'supported'—and similarly where 'adherence' or sphincteric action are the agencies of maintenance should aim at increasing or extending such effects. In practice, the methods must often be combined. The author's object appears to be to suggest investigation of methods for dealing with the symptomatology on the assumption that the displacement of viscera is associated with disturbance of the sympathetic plexuses, and based in large part on a consequent disorganization of the endocrine system. He feels that in this way even the most distantly connected phenomena, such as neuroses and dystrophies, may be rationally explained and treated by extensions of such methods as Taboulay's pericoeliac sympathectomy. E. R. C.

Rodi, G. Vie d'accesso alla regione celiaca per l'anestesia dei nervi splancnici e del plesso solare. [B.] [**Routes of access to the coeliac region for anaesthesia of the splanchnic nerves and solar plexus.**] *Arch. ital. di chir.*, 1921, **4**, 32.

Investigations on the dead body with non-diffusible injections lead to the conclusion that the needle, which should be 12 cm. long and enter from 8 to 10 cm. according to the development of the subject, must be entered 7 cm. laterally from the line of the spinous processes—and not, as hitherto advised by Kappis, 'at the lower margin of the last rib,' which is a variable point, but opposite the space between the spines of the 12th dorsal and 1st lumbar vertebrae. The inclination to the sagittal plane is about 45°. This injection, which should be from 40 to 50 c.c., will the better reach the semilunar ganglia and splanchnic trunks and coeliac plexus, the nearer the point of the needle approximates to the mid-line. It must be practised on both sides to be efficient. When it is necessary to anaesthetize the 2nd and 3rd lateral lumbar ganglia a further similar injection on each side should be made at the level of the 1st and 2nd lumbar interspinous space. E. R. C.

Segale, G. C. Sulla funzione motoria dell' intestino. [**On the motor function of the intestines.**] *Arch. ital. di chir.*, 1921, **4**, 101.

This paper, besides including a general discussion with bibliography, records the results of experiments on dogs and monkeys to demonstrate the absence of 'antiperistalsis'. By the adoption of an ingenious technique the author inverts a part, or the whole, of the small intestine without rotating the mesentery through 180°. All the cases of total reversal died within a few days, with evidence that the upper junction had been subjected to great internal pressure—enough in two instances to burst the suture line—and apparently, as others have found, the operation is incompatible with life.

The course of the cases of partial 'inversion'—i.e. of reversal of half to one metre of small intestine—was followed by radioscopy, and at the termination, which was invariably by emaciation after an initial increase of weight, by necropsy.

It appears that notwithstanding a continuance of the peristaltic wave in the usual direction—now adverse to the current—fluid or pultaceous contents pass through the inverted loop by virtue of the muscular effort in the coil above the upper anastomosis. This effort, however—even when reinforced by muscular hypertrophy of considerable degree, is insufficient to propel solid masses, which after swaying forwards and backwards in the reversed loop come to rest in a cumulative mass at the proximal (originally distal) end of the loop, there inducing a dilatation which ultimately attains large proportions, and is accompanied by thinning of the walls and eventual perforation. All the animals that did not die of starvation perished as a result of perforation peritonitis. It appears obvious that no reversal of direction of the peristaltic wave takes place—at least in the circumstances of the experiment. E. R. C.

Lusena, G. Stenosi pilorica da granuloma tubercolare. [B.] [**Stenosis of the pylorus by tuberculous granuloma.**] *Arch. ital. di chir.*, 1921, **4**, 1.

The author, who gives details of a personal case, abstracts also 66 cases from the literature and private communications. He recognizes four forms in which tuberculosis may produce stenosis: that predominantly ulcerative and mucosal in site; the infiltrating type; the form characterized by 'tumour' formation; and the extra-gastric, in which the obstruction is brought about by the pressure of lymph-glandular masses, or by bands and adhesions in the fibro-adhesive type of tuberculosis peritonitis. Whilst admitting that the majority of cases are not diagnosed before exploratory laparotomy, and perhaps not always then, Lusena writes with the object of facilitating recognition. *Sex* affords little help, for in 45 cases in which the sex is stated 21 were males and 24 females; the ulcerative form occurred in the proportion of 6 males to 1 female; the 'tumour' type in 5 males to 13 females. *Age*, on the other hand, is of importance, for 75 per cent. of the cases occur before 40, and even of the groups which present clinically a 'lump' 64 per cent. are under 40 and 44 per cent. under 30 years. Since many of these cases are diagnosed clinically as malignant, this point is important. At least half these patients show other evidence of tuberculosis, many of them in the lungs. In some cases with gastric lesions only, the cutaneous or ophthalmic reactions have been positive. *Haematemesis*, even in the ulcerative form, is not common. In more than 60 per cent. of cases free HCl was present; when it was absent, lactic acid was found.

Diarrhoea is sometimes observed, but not frequently. There may be evening fever and malaise, or night sweats. Blood examination furnishes nothing diagnostic. The author states that though emaciation and pallor are often marked, they are not of the genuine cachectic type, nor is there the characteristic disturbance of appetite met with in carcinoma. In the author's case—and possibly others—onset of the gastric symptoms was followed by the appearance of enlarged glands above the clavicle. A biopsy of one of these enabled him to make a definite diagnosis.

Surgical treatment, when recorded, seems generally to have been by gastro-enterostomy; the immediate results have been fairly good, but in many patients death has resulted in a few months from intercurrent tuberculous lesions. The author's own patient, who had only temporary benefit from a gastro-enterostomy, died three months later, and at the necropsy, in the centre of the tuberculous mass, was found a carcinoma apparently commencing in the site of the original tuberculous mucosal lesion.

E. R. C.

Sweetser, H. B. Splenectomy in third stage of Banti's disease. *Surg. Gynec. & Obst.*, 1921, **33**, 376.

Although many cases of splenectomy for splenic anaemia have been reported, but few have been so treated in the terminal stage. Sweetser was only able to collect forty-two cases. He has included in his analysis all cases presenting ascites as a complication of an enlarged spleen. Thus in forty-two cases there are seven of primary cirrhosis of the liver with ascites, three of syphilis with cirrhosis of the liver and ascites, one of thrombosis of the splenic and portal veins with enlarged spleen and ascites, and one of primary lymphosarcoma of the spleen with ascites. Eleven cases reported in 1908 showed a mortality of 72·7 per cent., but in the forty-two cases under review this was reduced to 26·5 per cent., and, since medical treatment shows 100 per cent. mortality, this must be regarded as very good. At least 55 per cent. of those which survived operation lived and remained in good health for more than fifteen months. Of the seven cases of primary portal cirrhosis of the liver five were greatly relieved. Even in 1914 Kidd commented on the clinical similarity of Banti's disease to primary cirrhosis of the liver, and asserted that all cases of hepatic cirrhosis with enlarged spleen should be treated by splenectomy.

Sweetser's case was a male of 37, who first became jaundiced in June 1919. In May of the same year he had haematemesis and melaena, which was repeated in June. On June 11 ascites was first noticed, and a diagnosis of either pernicious anaemia or cirrhosis of the liver was made. In July the abdomen was tapped, the fistula remaining open with very free drainage for twelve days. On August 11, 1919, the abdomen was much distended and the spleen extended to the level of the umbilicus and the midline. The liver was not palpable and its area of dullness was diminished. The Wassermann reaction was negative. An examination of the blood showed haemoglobin reduced to 60 per cent. and the red blood corpuscles 3,700,000. He was tapped several times, and on September 1 the spleen was removed. The gall-bladder was normal and the liver small and hard with a hobnail surface. After operation the ascites recurred rather slowly and the abdomen had to be tapped, but after this it did not again recur. There was a rapid increase in the number of white blood corpuscles. He left hospital on

October 24. Seen again on November 13, 1920, he was then apparently in perfect health. The liver dullness extended to the costal margin and there was no jaundice and no ascites. The haemoglobin was 85 per cent., the red blood corpuscles 4,980,000, and the leucocytes 8,650.

In many of the reported cases this relative lymphocytosis had been present. A. J. W.

Rous, P., and **McMaster, P. D.** **The concentrating activity of the gall-bladder.** *J. Exper. M.*, 1921, **34**, 47–73, 95. (*Brit. M. J.*, 1921, ii, 214.)

These are two companion papers in which the influence of the gall-bladder and bile-ducts respectively on the bile have been investigated. The first considers the effect of the gall-bladder in causing concentration of the bile and the other discusses the different characteristics of the bile which may be found when there is an obstruction of the ducts. Using the amount of pigment which was present as an indication of the concentration of the bile, the authors came to the conclusion that in a normal gall-bladder there is an extreme and very rapid concentration of the bile. In one case the amount of bile was reduced from 49·8 c.cm. to 4·6 c.cm. in twenty-two and a half hours. The fluid is absorbed but the pigment is not. They regard the gall-bladder, therefore, as an extremely valuable reservoir whose capacity may be considered as greatly increased owing to its power of rapid concentration; by this means it overcomes the great rise of pressure that may occur when the escape of bile is prevented by a spasmodic contraction of the sphincter of Oddi. They also lay stress upon the fact which has been for many years recognized, that the mucus in the bile is secreted by the gall-bladder and not by the liver. Although they recognize the fact that surgical removal of the gall-bladder is rarely followed by any ill effects, they utter a warning that such an operation may not be so uneventful as is usually considered.

In the second paper an attempt is made to discover the reason why in some cases when the common duct is obstructed the bile is dark and tarry while in others it is thin and mucoid and forms the so-called white bile. Their explanation is that if the contents of the duct have free access to a healthy gall-bladder the excess of fluid will be absorbed and the dark tarry bile, such as is usually seen, will be present. If, however, the cystic duct be also obstructed, or the gall-bladder be diseased to such an extent that it can no longer concentrate the bile, then the fluid will not be concentrated and the white bile will result. [Note by Abstractor: This explanation would not, however, seem to be completely satisfactory, for it is the experience of many surgeons that white bile may be found in cases of chronic pancreatitis or carcinoma of the head of the pancreas when the gall-bladder freely communicates with the common duct and its walls appear to be healthy. The change from the thick viscid material to the white bile would seem rather to depend upon the time and the extent of the obstruction, i.e. whether the liver has failed to secrete bile. Moreover, the characteristic white bile shows more than a lack of concentration. It is much paler and contains presumably far less than does the fluid which is normally found in the hepatic or common ducts.] A. J. W.

Sweetser, H. B. Injury of the bile-ducts and methods of repair. *Ann. Surg.*, 1921, **73**, 629.

Not only is interference with the flow of bile a most serious condition which, if left, will probably become fatal, but operative measures to restore the flow are sometimes associated with great difficulty. In the present communication obstruction from the pressure of malignant tumours is not considered, and the author finds in the remaining cases that it is due (1) to stenosis of the ducts following deep ulceration ; (2) to pressure by adhesions; (3) to division of the common duct, intentionally or accidentally. It is believed that accidental division is much more common than would be gathered from the literature, as probably many cases are not reported, and it is likely to become more common in future as cholecystectomy is replacing cholecystostomy. Eliot was able to collect 190 cases, 45 being from the Mayo Clinic, and Eisendrath has laid stress upon the anatomical abnormalities which are likely to endanger the ducts during operation. Sweetser reports one case in which division occurred at operation and was treated by immediate end-to-end suture of the ducts, but the patient did not recover. In a second case a cholecystectomy was followed by obstruction. There was at first a profuse flow of bile which later disappeared, the wound healed, and the stools were of a normal colour. Later jaundice occurred and a second operation was performed. A probe could not be passed down the common duct, but as there had been some bile in the stools the duct was simply drained. The second operation was followed by a permanent biliary fistula and a third operation was undertaken five months later. The proximal end of the duct was identified and was sutured round a tube into an opening made in the duodenum. The junction was augmented with an omental flap. Complete recovery followed.

A brief review follows of the methods that have been used to bridge a gap in the common bile-duct. A. J. W.

Walton, A. J. Reconstruction of the common bile-duct. *Brit. J. Surg.*, 1921, **9**, 169.

There are certain cases where the common bile-duct is obstructed or destroyed in which cholecystenterostomy is unwise or impossible. These cases may be considered under the following headings : (1) accidental injury and removal of a portion of the common duct in performing the operation of cholecystectomy ; (2) injury of the hepatic or common ducts owing to the absence of a cystic duct ; (3) certain cases of early chronic pancreatitis ; (4) certain cases of advanced chronic pancreatitis ; (5) combined carcinoma of the gall-bladder and common duct ; (6) some cases of carcinoma of the head of the pancreas ; (7) obstruction of the common bile-duct from scar tissue.

In the first three groups the common bile-duct is either of normal size or collapsed, while in the last four it may be considerably dilated. Stress is laid upon the frequency with which the common duct is injured and upon the fact that this is more prone to happen owing to anatomical abnormalities. A case of congenital absence of the cystic duct is described, although such a condition is often said not to occur.

The different operations that have been undertaken from time to time are then discussed. Direct suture is usually performed, but it may be impossible if the lower end of the duct cannot be discovered, and even if satisfactorily accomplished it is prone to be followed later by stenosis. Lateral choledoch-enterostomy is described, but has been found unsatisfactory at times owing to angulation of the duct.

Of the different methods of re-formation the most satisfactory is that of direct implantation of the end of the duct into the duodenum, and this should be carried out if possible. Sometimes, however, so little of the duct may be left that it may be impossible to draw the duodenum sufficiently high up to allow the formation of an adequate valve. It is for this type of case that the author has found his operation so useful. The steps of this operation are described: The upper end of the divided duct is laid bare and the duodenum drawn up as close as possible to it and sutured in position. A piece of tube about one and a half inches in length is sutured into the cut end of the duct with plain catgut, a flap of all thicknesses of the duodenal wall is now turned downwards and the resulting opening in the duodenum is sutured in its upper part, leaving only a sufficiently large opening to admit the tube. The lower end of the tube is passed into the opening of the duodenum and the flap turned upwards and sutured around the tube and the divided end of the duct. By this means a valvular opening is made.

The author has found that the operation is simple to perform, and the piece of tube, being only sutured with plain catgut, is passed about the tenth day.

For cases of low obstruction of the undivided duct a slight modification of the steps of the above operation is made. A lateral opening as low as possible is made into the dilated duct and a tube inserted into this and sutured in position. The remaining steps of the operation are as before, the duodenal flap being sutured around the tube and the side of the common duct laterally.

A detailed account of ten cases is given, four of which were treated by other than the reconstruction method with unsatisfactory results. There were three in which the new duct was joined to the end of the common duct with two recoveries, and three in which the new duct was joined to the side of the common duct, also with two recoveries. A. J. W.

NEUROLOGY

Stahl, R. Zur Pathogenese und Lokalisation der Polyneuritis. *Deutsche Ztschr. f. Nervenheilk.*, 1921, **72**, 129.

Stahl prefaces his paper with a short *résumé* of the various views held, since Leyden made his observations in 1875, as to the seat of the essential lesion in polyneuritis. Leyden believed that this was cellular, involving the nerve-cells of the spinal cord, but later, largely under the influence of Oppenheim, Strümpell, and others, the nerve-fibre degeneration has come to be regarded as the essential lesion.

This has been the state of opinion until very recently, when the discovery of an increased globulin content without pleocytosis in the cerebrospinal fluid has raised the question again.

Roemheld, Feer, Queckenstedt, and Walter have all made observations in this sense, and Walter has, in addition, found a localized round-celled infiltration of the meninges. The last-named points out that the distribution of sensory loss in polyneuritis is at the distal extremities of the limbs, a distribution difficult to correlate either with radicular or with peripheral nerve lesions. He finds that the sensory and motor disturbances are not always of the same relative intensity: sometimes one predominates, sometimes the other, and he concludes that the lesion must be situated at some point where sensory and motor fibres have not yet joined, namely, in the spinal roots; moreover, it is of inflammatory character.

Stahl has observed eleven cases of polyneuritis, three diphtheritic, and six of uncertain origin, and in all he finds a positive Nonne-Apelt reaction without any increase of cells in the cerebrospinal fluid. One of these cases died in the fifth week of the polyneuritis, which was associated with chronic suppuration. The motor cells of the cord and the posterior root ganglion cells all showed chromatolysis and eccentricity of the nucleus: Nissl's 'acute cell lesion'. There were no inflammatory changes in the ordinary sense of the word in the cord. The small blood-vessels in the spinal root ganglia and in the spinal roots showed round-celled infiltration of adventitia and media, while there was proliferation of the intima. The peripheral nerves were degenerated, and between the nerve-bundles there was some lymphocytic infiltration. Stahl concludes that the noxious agent concerned reached the spinal cord by the blood-vessels of the spinal roots, giving rise in this situation to an inflammatory reaction, which secondarily affected the nerve-fibres as they coursed through the roots and spinal ganglia. The lesions in the posterior root ganglion and the anterior horn-cells he regards as secondary to the nerve-fibre involvement. In short, the primary and essential lesion of polyneuritis is in the spinal roots.

It may be questioned whether the case in question was, as Stahl supposes, a typical one of polyneuritis. The patient was found at autopsy to have multiple septic foci, while the presence of endarteritis suggests syphilis as a causal factor. Many authorities, including Nonne, believe that syphilis does not give rise to polyneuritis in the ordinary sense of the term, and the asymmetrical distribution of the symptoms—the right arm appears to have been unaffected—rather indicates that Stahl's case was not typical. Moreover, we doubt whether any great stress can be laid upon the fact that the distribution of cutaneous sensory loss, which, after all, corresponds fairly closely with that of the motor symptoms, does not accord with what we know of peripheral sensory nerve distribution.

We have only to suppose that function is most disturbed in the longest nerve-fibres to explain the distribution of both sensory and motor disorders. This does not involve us in an assumption that the longest fibres are more severely hit than shorter fibres, but may be supposed to be due to the fact that impulses passing along long fibres which are undergoing pathological changes have a much greater length of decrement (to use Adrian's term and conception) to pass than when only a short length of diseased fibre has to be traversed. F. M. R. W.

LINDSTEDT, F. Zur Kenntnis der Aetiologie und Pathogenese der Lumbago und ähnlicher Rückenschmerzen. [**A contribution to the aetiology and pathogenesis of lumbago and other forms of back-ache.**] *Acta Med. Scand.*, 1921, **55**, 248–80.

Lindstedt's thesis, in support of which he gives the following statistical data, is to the effect that sciatica, lumbago, and other forms of backache are to be regarded as reflex neuralgias, arising in the same way as trigeminal neuralgia due to dental caries, sinusitis, otitis, and the like. This reflex mechanism can be set going not only by direct painful impulses but also by local muscular hyperfunction, such as is provoked by excessive walking or by static deformities like flatfoot. If this hypothesis is correct, sciatica, lumbago, and the like should be far more common in persons suffering from the following ailments than in healthy persons. (1) Marked deformities of the spine, (2) diseases of the pelvis and the neighbouring structures (severe appendicitis, hernia, varicocele, and other conditions causing discomfort or pain on walking), (3) diseases of the hip-joint or thigh, (4) traumatic and other diseases of the knee associated with effusion and confinement to bed, (5) genu valgum, (6) genu varum, (7) genu recurvatum with marked relaxation of the capsule of the joint, (8) injuries to the foot, (9) severe flatfoot, (10) other morbid conditions of the foot such as pes varus and hallux valgus, (11) persistent or relapsing polyarthritis, (12) marked varicosity of the veins, (13) 'general static weakness', (14) fractures below the knee, (15) other severe disorders of the soft tissues. In a second category are placed similar but less severe conditions, and in a third category practically healthy persons are placed. As the following table shows, 1,578 recruits were examined for the morbid conditions mentioned in the above list and for present signs or a history of sciatica or lumbago.

	With Lumbago.	Without Lumbago.	Total.	Sciatica.
(1) Severe disorders	78 (24.5 %)	240 (75.5 %)	318 (100 %)	11 (34.6 %)
(2) Slight disorders	24 (6.1 %)	372 (93.9 %)	396 (100 %)	2 (5.1 %)
(3) Normal	15 (1.7 %)	849 (98.3 %)	864 (100 %)	1 (1.2 %)
Total	117 (7.4 %)	1,461 (92.6 %)	1,578 (100 %)	14 (8.8 %)

It will thus be seen that lumbago was 14 times more frequent among recruits subject to one or more of the diseases referred to than in perfectly healthy recruits. The incidence of lumbago among recruits subject to minor ailments took an intermediate position. It will be noted that there were only 15 cases of lumbago among the perfectly healthy recruits, and even in these cases Lindstedt thinks that there was probably some morbid process overlooked, such as spina bifida occulta, which gave rise to a reflex expressing itself as lumbago. He does not deny the importance of psychic depression, infection, toxaemia, cachexia, meteorological influences, and the like, but he attaches special importance to a constitutional neurosis as an auxiliary to the above-mentioned exciting causes. C. L.

Morris, M. L., and Jacobson, V. C. Acute ascending myelitis of infectious type. *Arch. Neurol. & Psychiat.*, 1921, **6**, 509.

The authors report a case of acute ascending poliomyelitis and one of acute ascending myelitis, both fatal. In the former case, the paralysis when first observed was confined to the legs and was not complete. On the following day there was total flaccid paralysis of both lower limbs and weakness of abdominal and chest muscles. Later the paralysis ascended still further, involving the arms, and death took place from diaphragmatic and respiratory muscle paralysis. All tendon-jerks were abolished and there was no sensory loss. Subsequent examination revealed typical lesions of acute anterior poliomyelitis. The second case was that of a healthy young male adult, who was taken acutely ill with vomiting, headache, delirium, and pain in the back. On the third day there was complete paralysis from the hips downwards with retention of urine. Below the level of the sixth rib there was complete sensory loss. On the fourth day there was flaccid paralysis of both arms, and death occurred with signs of brain-stem involvement. Subsequent examination revealed an acute diffuse ascending myelitis. The cord was soft, oedematous, and congested, and it was difficult to differentiate white from grey matter by the naked eye. The lung, spleen, and kidneys were normal. There were several small areas of necrosis in the liver. The most marked spinal lesions were in the grey matter. There was acute nerve-fibre degeneration, and numerous small haemorrhages in the lateral columns. The anterior horn-cells were relatively less severely affected. There were various grades of chromatolysis and a moderate degree of round-celled infiltration. The aetiology of the condition was not determined. The cerebrospinal fluid contained excess of cells but was sterile as far as could be determined. The case occurred just before the outbreak of an epidemic of poliomyelitis, and the authors discuss the possibility that the infection was one by the organism of this disease; they incline to accept this explanation of the case, and believe that a change of type in poliomyelitis is just as probable as in other diseases. F. M. R. W.

Cadwalader, W. B. Observations on character of the onset of spinal paralysis with reference to the significance of the apoplectiform type of onset in contrast to the slow progressive development of paralysis. *Arch. Neurol. & Psychiat.*, 1921, **6**, 541.

The mode of onset of a paralysis of spinal origin may give valuable information as to the nature of the pathological process concerned. Extramedullary spinal tumours are usually of slow growth and give rise to slowly progressive paraplegia in which symptoms of spinal root irritation are prominent, in fact pain may be present before signs of compression of the cord can be detected. In addition there may be pain in the paralysed legs. This pain is of central origin, like that described by Gordon Holmes as occurring in cases of gunshot wound of the cord (*Medical Science*, 1920, **2**, 355). It may be due to circulatory disturbances in the affected area of the cord. The development of motor weakness is very insidious, and intermissions, such as occur in disseminated sclerosis, are very rare. The author says nothing as to the order of appearance of motor, sensory, and sphincter symptoms in gradual compression of the cord.

In striking contrast to these cases are cases of thrombosis of spinal arteries. Here the onset is sudden and paralysis becomes total within an hour in some instances. Such thromboses are commonly syphilitic. Many cases of so-called acute myelitis are of this nature. The acute ataxia of posterior column lesions, when these are of sudden development, may give rise to what is superficially a sudden motor paralysis. Traumatic haemorrhage into the cord is another common cause of sudden paraplegia. Several case records are appended. An interesting point brought out by Cadwalader is that in cases of acute myelitis so-called, the essential factor is a sudden interference with the blood-supply to one or more segments of the cord, with rapid softening. F. M. R. W.

McKendree, C. A., and **Imboden, H. M. Ossification of the meninges.** *Arch. Neurol. & Psychiat.*, 1921, **6**, 529.

The authors preface their paper with a brief historical review of the subject. They find that the falx cerebri is the commonest situation of osteophytic growth, especially alongside the superior longitudinal sinus. Next in frequency of involvement is the tentorium. Usually the dura alone is involved, but the pia-arachnoid may be secondarily, or even in some instances primarily, affected. The meninges may be the seat of scattered isolated plaques, which vary in size and form from small flakes to nodules the size of a hazel-nut, which mould the underlying cerebral convolutions. The external surface of such masses is smooth and shiny, but the mesial aspects are invariably rough and jagged. Occasionally stalactite-like processes grow inwards, piercing the cortex. In many instances a process of true bone formation is in question.

A case of extensive ossification of the meninges with clinical symptoms is recorded. The patient was a woman of 49, who for nine years had suffered from periods of nausea and vomiting, with diffuse neuralgic headaches and sleeplessness. Examination revealed no definite objective signs, though the tendon-jerks on the right side are said to have been increased, and there was some doubtful weakness of the left lower face. There was no optic neuritis. X-ray revealed extensive ossification of the meninges.

F. M. R. W.

Thomson, A. P., and **Piney, A.** **A case of decerebrate rigidity in an infant** *Lancet*, 1921, ii, 1105.

Jefferson, C. **Bilateral rigidity in middle meningeal haemorrhage.** *Brit. M. J.*, 1921, ii, 683.

Jefferson describes two cases of middle meningeal haemorrhage associated with marked rigidity of the limbs. In the first case, the patient, when seen, lay unconscious with the arms rigidly extended and adducted, the forearm pronated, and the hands clenched. The legs were extended and adducted, the feet inverted and plantarflexed. There was Cheyne-Stokes respiration, and at the height of respiratory activity the tone definitely increased. Ankle-clonus and a dorsiflexor response of the hallux were present on both sides. Any attempt at passive movement of the limbs caused marked access of rigidity and a fine tremor. The head and eyes were deviated to the left. The pulse-rate was 60. Operation revealed a fracture through the wall of the left temporal fossa and free bleeding from the middle meningeal artery. A large extradural clot, 12 cm. in length and 4 cm. in thickness lay over the left hemisphere. Death followed in three hours. In the second case, the symptoms were similar, with the exception that the left arm was partly flexed. The patient was profoundly comatose and was subject to 'tonic seizures' consisting of sudden accesses of rigidity. As in the first case, these occurred at the height of periodical respiration and were accompanied by twitching of muscles. Operation revealed a large depressed fracture of the left frontal bone and an extradural clot of considerable bulk. In both cases also there were severe associated lesions of the frontal lobe.

Jefferson regards the tonic spasm as the effect of circulatory disturbances in the brain, which result in paralysis of function in the highest levels of the brain, with release of lower level activities. He carefully refrains from labelling the condition decerebrate rigidity, but regards it as similar to the clinical picture described by Wilson and so named (*Medical Science*, 1921, **4**, 55).

Thomson and Piney's case was one of cortical encephalitis in a child of four months. The illness lasted for two months and terminated in death. During this period the child was apparently unconscious and lay rigidly extended in opisthotonos with head retraction. The legs were rigidly extended and adducted, the feet plantarflexed. The arms were similarly extended, the forearm pronated, and the fingers flexed at the metacarpo-phalangeal joints only. There is no note as to the condition of any of the reflexes. The rigidity was intense and varied but little during the course of the illness. Ultimately the feet became rotated outwards and dorsiflexed. Post-mortem examination revealed extensive softening of the cerebral cortex and of the immediately subjacent white matter. The basal ganglia and brain-stem appeared normal. The cortical vessels were diffusely calcified and obliterated. The authors regard the condition as decerebrate rigidity 'of the type to be expected after ablation of the cortex'.

The principal interest of these cases consists in the suggestion that they may correspond to the condition of decerebrate rigidity described by Sherrington in animals after transection of the brain-stem. Within the past twelve months no less than four papers have appeared in which various forms of rigidity following cerebral lesions have been so identified. It is clearly of considerable importance that we should be able to correlate experimental with clinical observation, and to interpret the latter in the light of the former. However, unless we are to be seriously misled, the correlation must be most carefully made. We can never expect to see decerebrate rigidity produced in man by a lesion comparable with that employed to produce it in animals, but we can form a conception as to whether the lesion of disease fulfils the necessary conditions. Simple removal of cortical influence does not, as Thomson and Piney suppose, suffice to produce decerebrate rigidity. Sherrington, Thiele, Weed, and Magnus have found that it is necessary for the plane of section to fall caudal to the anterior colliculi. An animal with its brain-stem transected at the anterior limits of the midbrain does not show any tonic spasm in its musculature. Part at least of the midbrain must be removed. It seems possible that the red nucleus and the superior cerebellar peduncle have to be taken away before rigidity develops. Therefore, while decerebrate rigidity is certainly a 'release' symptom, certain brain-stem centres as well as the motor cortex have to be put out of action before this release can occur. This, presumably, is why purely cortical hemiplegias are not spastic. On the physiological side accurate criteria are equally essential. The decerebrate rigidity described by Sherrington has certain well-defined qualities, and rigidities not possessing these cannot rightly be identified with it. Yet in none of the papers mentioned has an attempt been made to study anything but the attitude of the limbs. Whether or not the spasm shows plasticity, a selective distribution, or is governed by reciprocal innervation has not been investigated. Moreover, the variety of clinical pictures already included under this designation indicates that there has been no clear guiding conception of what a very definite condition true decerebrate rigidity is, and the term bids fair to become a vague label including all obscure forms of tonic spasm in a category which has a thoroughly false air of scientific precision.

In one of his early papers on the subject, Sherrington pointed out that 'decerebrate rigidity is but a type of extensor spasm of which allied examples follow various other lesions in the cerebello-cerebral region'. So that it does not follow that all forms of extensor rigidity observed clinically are true decerebrate rigidity. Under the loose standards which are being adopted clinically, strychnine spasm might well be included as decerebrate rigidity, but we know that it is something very different. All the limb and trunk muscles are in spasm, there is no reciprocal innervation and no 'shortening reaction'.

Moreover, the occurrence of the so-called 'tonic fits' in many of the clinical cases so described, should surely make us hesitate before we can regard the condition even as a release phenomenon. It is infinitely more probable that tonic fits are manifestations of hyper-excitability of nervous mechanisms, or, to use a better-known term, are 'irritative symptoms'. The conditions of vascular disturbance under which they often occur, notably in Jefferson's cases, make this extremely probable. All these possibilities will have to receive far more attention than they appear to have done, and we must exercise great caution before accepting the diagnosis of decerebrate rigidity for forms of extensor spasm seen in man.

F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Michaelis, L. Die Prüfung der Alkalität in Nährböden. [**The determination of alkalinity in media.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **32**, 194.

The question of the alkalinity of broths is here revived. The author considers the use of the hydrogen electrode to be too complicated for general use in the laboratory. It is due to this fact that Sörensen's indicator method was introduced. Clark has improved on this by the adoption of a series of indicators. Gillespie employs an indicator method using Clark's indicators, but without buffers. Michaelis objects to the use of two-coloured indicators. Instead, he has devised a technique based on a one-coloured indicator, viz. 0·3 gm. m-Nitrophenol in 100 c.cm. distilled water. He says the method is much simpler than others and is not less accurate. The indicator changes from colourless to yellow. But since broth is itself of a yellow tint, the difficulty has to be overcome by two artifices. One is the dilution of the broth with 0·85 per cent. saline. This, he proves, does not alter the P_H value, owing to the broth acting as a buffer in virtue of its peptone and phosphate capacity. The dilution, however, diminishes the colour, but does not remove it. A second artifice is therefore used. This consists in an application of the principle used by Walpole in his comparator (*Biochem. J.*, 1910, **5**, 207). The author, however, employs a modification of this comparator devised by Hurwitz, Meyer, and Ostenberg, and described in Clark's book (W. M. Clark: *The Determination of Hydrogen Ions*, Baltimore, 1920). Michaelis claims that the optical advantage of the two-coloured indicators of Clark can, by means of the above technique, be transmitted to the one-colour indicator. Details are given of the preparation of the indicator solution, the use of the comparator, and the setting up of a series of standard tubes of P_H values ranging from 6·8 to 8·4. The P_H value of any prepared bouillon can be quickly and accurately determined. It can equally well be used for agar and gelatin.

W. A. M. S.

Deussen, E. Die Gramsche Bakterienfärbung, ihr Wesen und ihre Bedeutung. [**Gram's stain, its nature and significance.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 512.

This is a study intended to elucidate the essence and cause of Gram's staining. Working with yeast-cells and Yoghurt bacilli, the author found that they can be deprived of their property of staining positively by Gram's method by a 4 per cent. solution of sodium hydrate, the exact technical details of his method being described. By addition of nuclein or nucleic acid to the organisms thus rendered Gram-negative a positive Gram stain may be regained. Apparently the dead cell membrane is permeable for nuclein and nucleic acid in the form of their combination with sodium salts, although these same salts are not able to dialyse through parchment or pig's bladder.

W. B.

Pergola, M. La ricerca del bacillo difterico e la cultura di arricchimento. [**On the cultivation and enrichment culture of *B. diphtheriae.***] *Pathologica*, 1921, **13**, 113.

Potassium tellurate is very suitable for investigations regarding *B. diphtheriae*, but chiefly for the enrichment of its cultures. The reagent should be added in the proportion of 1:5,000 to the solid and fluid media generally used for cultivating *B. diphtheriae*. For the staining of smears from successful cultures the following method is particularly recommended: (1) Stain as usual with Neisser's acetic methylene-blue solution. (2) Wash in water. (3) Treat for 10 seconds with Lugol's fluid. (4) Wash. (5) Stain for 10 to 15 seconds with a 1:300 solution of chrysoidine prepared with boiling water and filtered.

C. d. F.

Segale, M. Sui vari tipi di meningococco. [**On the various types of meningococcus.**] *Pathologica*, 1921, **13**, 311.

A methodical research carried out on 11 strains of meningococcus isolated and collected through many years in the Laboratorii scientifici Galliera, Genoa. The fresh investigations of the author showed that, in spite of differences in their agglutinating power, the cultural and biochemical properties of the 11 strains were the same. The chief of these common characteristics were: (1) The fermentation of dextrin, and, in a smaller degree, of levulose. (2) The inhibited development after treatment with bile. (3) The resistance to very great dilutions of optochin (1:40,000).

A study of the agglutinating properties of the 11 strains made by means of original sera led to the conclusions: (1) That Nicolle's type A corresponds to Gordon's type III. (2) That Nicolle's type B corresponds to Gordon's type II and to the Rockefeller paratype. (3) That Nicolle's type C corresponds to Gordon's type IV. No corresponding type was found, among the 11 strains, for Gordon's serum I and the Rockefeller regular serum. One of the strains investigated showed reversible agglutinating properties, its cultural and biochemical characteristics remaining unchanged.

C. d. F.

Williams, Anna W., and **Povitzky, Olga R.** **Growth of *B. influenzae* without the presence of haemoglobin.** *J. Med. Res.*, 1921, **42**, 405.

In recent years a considerable amount of work has been directed towards the elucidation of the curious growth requirements of *B. influenzae*.

In particular, efforts have been made to grow the bacillus in the absence of blood-pigment, considered by Pfeiffer and most other workers to be essential. It has always been known that certain bacteria (staphylococcus, *B. diphtheriae*, and many others) have a marked stimulating action upon the growth of the influenza bacillus, but only, according to most authors, in the presence of blood-pigment. Williams and Povitzky, however, having published a previous paper upon the subject, consider 'that this was one of those questions that might be accepted as settled' in favour of the growth without pigment. Taking ordinary agar, or, to exclude any possibility of blood-pigment in the medium, wheat agar, they carried a number of strains of *B. influenzae* through 22 subcultures, stimulating the growth with gonococcus, *B. diphtheriae*, and other bacteria. It would appear that the growth obtained is a mixed 'mass' culture without isolated colonies.

P. F.

Armstrong, R. R., and **Gaskell, J. F.** **Studies on the pathology of pneumococcal infections of the human lung.** *J. Path. & Bacteriol.*, 1921, **24**, 369.

This paper deals with the manifestations of pneumococcal infections in the lung both by investigation of *post mortem* material in man and by experimental material in rabbits. The authors consider that the pneumococcus invades the lungs by the air-passages, the blood-stream, and the lymphatic channels. The aerogenic infections include both lobar pneumonia and broncho-pneumonia, the infection settling in the bronchioles in both instances. The factors which determine the type of lesion are the virulence of the pneumococcus and the resistance of the host. Mechanical factors may also play a subsidiary part. The reaction of the pulmonic tissues is essentially the same in both forms of infection. There is nothing particular in the exudate of either form. In lobar pneumonia the pneumococci are mostly destroyed by the fifth day, so that endotoxin ceases to be liberated. Haematogenous infections give rise to a form of pneumonia called 'miliary', the infection spreading into the alveoli from the capillaries. The bronchioles are involved only secondarily. From the study of certain relapsing pneumonias in children the authors also believe in injection by way of lymphatic channels. After intratracheal insufflation of pneumococci in rabbits, lesions comparable to lobar and broncho-pneumonia were produced depending apparently on the virulence of the infecting pneumococcus. W. B.

Schnabel, A. Die Blutgifte der Pneumokokken. [**The blood poisons of pneumococci.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 175.

This is an investigation into the question of the blood-destroying poison produced by *Pneumococcus* and *Streptococcus mucosus*. The haemoglobin is converted into methaemoglobin, the process depending upon the number of bacteria and an optimal temperature of 37° C. The author believes that the methaemoglobin-producing substance is free, as is shown by the fact that the conversion of haemoglobin takes place better with bouillon cultures than with agar suspensions which have been washed. Further, optochin and sodium glycocholate, even in strong concentrations, produce no definite change in the production of methaemoglobin. The filtrate from bouillon cultures also effects the change in the blood. There is some evidence for the assumption that the methaemoglobin-producing product exerts an antagonistic influence on the haemolysis produced by pneumococci. W. B.

Thjøtta, T., and **Sundt, O. F.** **Toxins of Bact. dysenteriae, Group III.** *J. Bact.*, 1921, **6**, 501.

This is a study of the toxins produced by *B. dysenteriae*, Group III. This Group III, it may be stated, was previously differentiated by Thjøtta and Sonne, and contains bacteria which form acid in mannitol, maltose, glucose, and as a rule in sucrose. It does not produce indol and it grows in colonies with an irregular crenated edge. According to Sonne it is toxic to a milder degree for rabbits and monkeys than *B. shiga*. Filtrates of 8-day bouillon cultures of *B. dysenteriae*, Group III, are shown by the authors to contain a neurotoxin which exerts its effects after an incubation period. No intestinal lesions were encountered. The bacillus also possesses an endotoxin which causes intestinal disturbance, usually of a mild character. Repeated injections of the two toxins render animals immune, both sera showing a weak protective action against the homologous toxins. W. B.

Anzilotti, G. Ricerche sperimentali sulle lesioni articolari da bacillo di Eberth. [**Experimental investigations on articular lesions caused by *B. typhosus*.**] *Pathologica*, 1921, **13**, 387.

By means of intra-articular inoculations of living cultures of *B. typhosus* it is possible to cause in rabbits histopathological alterations in every way similar to those of arthritis deformans. Such lesions are fully developed about six months after the beginning of the experiments, by which time the inoculated bacilli have been completely eliminated. C. d. F.

Cannon, P. R. **The effects of diet on the intestinal flora.** *J. Infect. Dis.*, 1921, **29**, 369.

This experimental research was undertaken to test to what extent diet is a factor controlling the activities of bacteria in the intestinal tract, and especially from a quantitative point of view. Rats and human beings were tested, the faeces being examined microscopically and on various media for the colon-acidophilus ('C–A') ratio, the production of hydrogen sulphide, &c. The general results confirm those previously obtained by Kendall, Rettger, Torrey, and others, viz. that grain foods, lactose, and dextrin, when fed to rats in proper proportions, lead to a marked predominance of aciduric bacteria, whereas animal proteins encourage gas-producing proteolytic types both aerobic and anaerobic. Vegetable proteins and certain starchy foods do not encourage the development of proteolytic types to the same extent as animal proteins, and in many cases indeed exert a definite antiputrefactive influence, favouring the development of *B. acidophilus* and suppressing hydrogen-sulphide formers and sporing bacteria. In the human experiments, extending over a period of ten days, a diet of bread, milk, and lactose caused a marked development of aciduric bacteria. In one experiment of the same duration a diet rich in vegetable protein brought about a predominance of aciduric bacteria with the elimination of anaerobic spores. W. B.

Kwaśniewski. Ueber die Ansiedelung des Typhusbacillus in der Gallenblase und Leber, die durch ihn erzeugten Gewebsveränderungen, mit Bemerkungen zur Chemotherapie der Typhusbacillenträger. [**On the localization of typhoid bacilli in the gall-bladder and liver and the lesions induced, with observations on the chemotherapy of typhoid carriers.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 252.

The author gives the result of pathological and bacteriological investigations into nine cases of typhoid and one case of *paratyphoid* B, the special object of his study being to determine by what route the gall-bladder is invaded and to what extent the liver and gall-bladder are injured. He believes in a primary haemogenic infection and produces evidence in support of the view that typhoid bacilli act on the liver-cells, inducing degeneration, while proliferative changes are set up in the gall-bladder, although he is unable to explain why these changes occur in some cases and not in others. He considers that methods of disinfection of carriers must aim not only at the gall-bladder but also at the liver, in which the bacilli are also to be found. The problem of chemically influencing the gall-bladder in the case of carriers is also complicated by the fact that typhoid bacilli may maintain a foothold in the marrow of the bones for years. W. B.

Fraenkel, Eugen. Über Roseola paratyphosa. [**On paratyphoid roseola.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 372.

From a careful study of the roseolae in cases of paratyphoid fever the author shows that, as in the case of typhoid, they are bacterial metastases in the lymphatic vessels of the skin. The roseolae may last for as long as 18 days before there is the slightest histological evidence of retrogression. In one instance repeated blood cultures showed no evidence of paratyphoid bacilli although they were found in the faeces and the patient's serum had a high agglutinating titre for paratyphoid B. An excised papule showed abundant bacilli. W. B.

Konno, T. Beobachtungen über eine sogenannte Mutationserscheinung bei dem schleimigen Stamme von Paratyphus-B Bazillen. [**Observations on a so-called mutation phenomenon in a mucoid strain of *B. paratyphosus* B.**] *Tohoku J. Exper. M.*, 1921, **2**, 159.

The author has made a study of certain slimy colonies isolated from a pure culture of *B. paratyphosus* B. Cultures made from a slimy colony gave two kinds of colonies, the one half-slimy, coarsely granular, the other not slimy at all although coarsely granular. From the first half-slimy colonies arise non-slimy granular colonies, while the non-slimy colonies always breed true. The agglutination reactions of the different colonies were studied. W. B.

Gildemeister, E. Ueber das d'Herelle'sche Phänomen. [**On the d'Herelle phenomenon.**] *Berl. klin. Wchnschr.*, 1921, **58**, 1355.

The author confirms the statement that in filtrates from stools a lytic agent can be obtained which acts on typhoid, dysentery, and colon bacteria, and can be transmitted by passage. He finds that the lytic action is not specific, and can also be obtained in the colony variants which appear in plates made from cultures exposed to the so-called 'bacteriophage'. He has also found it in the colony variants obtained from stools. He does not believe in d'Herelle's theory that the lytic agent is living, but agrees more with Bordet and Ciuca that d'Herelle's phenomenon is to be classed in the domain of bacterial variability, a view also shared by Bail (1921).

W. B.

Fasiani, G. M., e **Pachner, E.** Contributo alla sistemazione di alcuni anaerobi agenti di gangrena gasosa. [**On the systematization of some anaerobic germs causing gas gangrene.**] *Pathologica*, 1921, **13**, 231.

Investigations were carried out with the following strains: (1) *B. oedematiens* No. 145 of Weinberg and Séguin. (2) *B. bellonensis C. d.* of

Sacquepée. (3) Strain *G. 35* of Aschoff. (4) *B. of Novy 2 Y* supplied by Fasiani. The results obtained are summarized by the authors about as follows: (*a*) The strains investigated show some morphological differences by means of which they can, up to a point, be distinguished one from the other. The strain of Sacquepée is thin and slender; that of Aschoff thick and short. The strain of Weinberg and Séguin is similar to that of Sacquepée; that of Fasiani to Aschoff's strain. (*b*) The formation of spores and the form and situation of the latter are about the same in the case of all four strains. Their motility is evident when they are examined in the exudates of animals experimentally infected. (*c*) The cultural characteristics in Tarozzi's broth and the property of forming deep colonies in agar are common to all of them. Aschoff's strain often grows into filamentous colonies. (*d*) *B. oedematiens*, *B. bellonensis*, and strain *2 Y* coagulate milk rather slowly with separation of a woolly clot after 2 to 5 days. Aschoff's strain causes a rapid and intense fermentation of the milk, with production of much gas. The former three barely grow in congealed blood, while the latter liquefies this medium. (*e*) The lesions experimentally obtainable in guinea-pigs by means of the four strains are about the same. However, the oedema caused by Weinberg's and Séguin's strain is almost colourless and accompanied by a scanty production of gas; the other three cause a more or less haemorrhagic oedema with a pronounced production of gas. (*f*) The pathogenic properties of the four strains are neutralized by both the immune sera of Weinberg and Séguin, and of Sacquepée, but not by the common serum prepared for other anaerobic species such as *B. oedematis maligni* of Ghon and Sachs, and *B. perfringens*.

In consideration of these results the authors propose to subdivide the agents of gas gangrene into three groups: (1) Group of *B. perfringens* or *B. phlegmonis emphysematosae*. (2) Group of *B. of Ghon and Sachs* or *Vibrion septique*. (3) Group of *B. of Novy*, this to comprise *B. oedematiens*, *B. bellonensis*, and *B. der Gasoedem*. C. d. F.

Perazzi, P. Sulla sorte di alcuni stipiti di germi sporigeni introdotti nel sangue circolante. [**On the fate of certain spore-bearing microbes introduced into the circulating blood.**] *Pathologica*, 1921, **13**, 293.

Experiments were made by means of four strains of anaerobic germs, of which two were isolated from the blood of two subjects dead of puerperal septicaemia, and two from two cases of abortion with high temperature. The bacteria disappeared from the blood of these last two patients almost immediately after the emptying of the uterus. The isolated strains were in two cases *B. perfringens*, in one the same germ associated with *B. proteus* (? *vulgaris*), in one the Pasteur's *V. septique*. The 24-hour broth cultures were centrifuged, and the sediment, made into an emulsion with physiological salt solution, inoculated intravenously in healthy dogs and in others previously treated with an intravenous injection of 20 c.cm. of a 10 per cent. solution of peptone. The blood of the inoculated dogs was collected directly from one of the carotids at intervals of 15 minutes, starting five minutes after the inoculation and continuing up to the end of the second hour. It was bacteriologically and histologically examined with the following results: (1) Spore-bearing germs are rapidly eliminated from the circulating blood. (2) Masses of blood-platelets surround them and help in their 'fixation' in various organs such as the spleen, liver, and kidney. (3) The rapidity with which the germs are eliminated is in relation to their greater or smaller property of modifying the 'plasmatic equilibrium of the blood'. (4) The disappearance of the germs from the circulating blood is not due to an agglutination in Bull's sense (*J. Exper. M.*, 1914, **20**, 237; 1915, **22**, 484; 1916, **24**, 25) but to their immobilization and precipitation, these two phenomena being, in their turn, subordinate to the adhesion of the germs to blood corpuscles, to cells of the wall of blood-vessels, and chiefly to platelets. C. d. F.

Hall, I. C. Criteria in anaerobic fermentation tests. *J. Infect. Dis.*, 1921, **29**, 321.

Experimenting with pure cultures of pathogenic and non-pathogenic anaerobes, the author discusses the question of the criteria to be considered in estimating the fermentative powers. While the vigorous production of gas is generally considered as an indication of fermentation, he points out that two sets of facts may confuse the utilization of gas as a measure of fermentation for (1) it may come from simple sugars which are present in the medium, and which have survived the destruction by the bacteria (*B. coli*) employed to remove it; (2) it may come from proteins. The utility of titrable acidity as a criterion of fermentation is limited to media not containing coagulable proteins, the hydrolysis of which by proteolytic bacteria greatly increases the buffer capacity of the titrated samples. The author regards the increase in hydrogen-ion concentration as the best evidence of fermentation. No direct quantitative determination of hydrogen-ion concentration was found to be possible, although litmus was useful for quantitative work. W. B.

Randall, S. B., and **Hall, I. C. The use of *B. welchii* in the preparation of sugar-free culture medium.** *J. Infect. Dis.*, 1921, **29**, 344.

For many years cultures of *B. coli* have been used for the elimination of the so-called 'muscle sugar' from media intended for the study of fermentation reactions of bacteria. The authors have compared *B. coli* in this respect with *B. welchii* and an organism, *B. saccharolyte*, apparently isolated originally by Ernst in 1911, and they came to the conclusion that the best criterion of sugar-splitting was provided by an increase in hydrogen-ion concentration. As a result of their observations they recommend the use of *B. welchii* for the preparation of sugar-free broth. Most bacteriologists have regarded the sugar as effectively removed from a medium when it fails to produce gas on refermenting with *B. coli*, but by cross-fermentations the authors have shown that *B. welchii* is still able to produce acid and gas from media presumably exhausted with *B. coli* or *B. saccharolyte*. These latter are, however, unable to produce either acid or gas from media fermented with *B. welchii*. The time required for elimination of sugar by *B. welchii*, *B. coli*, and *B. saccharolyte* is approximately the same. While the 'sugar-free' broth produced by *B. welchii* filters through paper more slowly than that fermented by the two other bacteria, its filtrability improves as the culture ages, and the product is always clearer than that obtained with the other bacteria. W. B.

Heller, Hilda H. Principles concerning the isolation of anaerobes. *J. Bact.*, 1921, **6**, 445.

This is a general discussion on the principles involved in the isolation and maintenance of anaerobes, the authoress finding: (1) that success depends more upon the critical sense of the worker than upon the method employed; (2) microscopic examination should be made on the original material, and of cultures after 24 and 48 hours' incubation; (3) heating of material should be carried out according to the requirements of the material; (4) chopped ox heart preferably containing a little peptic digest broth with a reaction of P_H 7·2 is a good routine medium; (5) selective media should be used for special purposes; (6) isolation by means of guinea-pig inoculation with subsequent cultivation from the heart, blood, or lesions may be used for pathogenic anaerobes, but cannot be depended upon to give a true picture of the pathogenic flora in the inoculum; (7) dilution in shakes of deep agar is preferable to any other method; (8) a medium for dilution 'shakes' should afford an opportunity for the growth of as many colonies as possible; such a medium being peptone-liver-agar; (9) when once pure a culture should be kept pure, autoclaved media only being used. Re-incubation, prolonged incubation in closed jars, storing in closed cans or dusty places should be avoided. W. B.

Murstad, E. Tetanus efter operationer. [B.] [**Tetanus after operations.**] *Med. Rev.*, 1921, **38**, 358–402.

After four cases of post-operative tetanus had occurred at a hospital in Bergen, the 'sterilized' catgut in use at this hospital was examined at Gade's Institute, where spore-forming germs were found on anaerobic bouillon culture. Injection of these cultures provoked fatal tetanus in mice. This catgut had been treated for 30 minutes at a temperature of 100° C. with absolute alcohol under pressure. Murstad has collected 189 published cases of tetanus following an operation, and though a strikingly large proportion of these operations (163 out of the 189) concerned the reproductive organs and herniae, it is improbable that the hypothesis of auto-infection is sound: if it were, tetanus should be comparatively frequent after operations on the intestine, but this is not the case. Murstad has carried out experiments with catgut, treated with 1 per cent. gentian violet, in various concentrations of alcohol. The gut was then embedded in paraffin, and the degree of penetration of the gentian violet was studied in sections. Even after three days' treatment, absolute alcohol had not penetrated to the interior. Alcohol concentrations, ranging from 60 to 96 per cent., had penetrated slightly, but it was not till the alcohol concentration was 40 per cent. or less that the penetration was effective. These findings indicated the use of alcoholic solutions not stronger than 40 per cent., but as catgut swells in so weak a solution of alcohol, this sterilization process is unsatisfactory. A series of tests with catgut artificially infected with tetanus spores showed that these could still be demonstrated after the gut had been treated by the following methods: v. Bergmann-Schimmelbusch's (sublimate-alcohol), Kümmel's (sublimate in aqueous solution), Brandt's (boiling in sublimate-alcohol), Bloch's (carbolic acid in aqueous solution), Dowd's (boiling in 97 per cent. alcohol under pressure), Åkerblom's (olive oil heated up to 150° C.), Reverdin's (heating in dry air for four hours at 140° C.). Living tetanus bacilli could not be found in catgut after treatment with one of the following methods: Hofmeister's (boiling in water catgut previously hardened in formalin), Claudius's and Rovsing's methods. These last two methods also fulfil other conditions required of perfectly satisfactory catgut. Claudius's method consists of leaving the catgut for eight days in a solution containing 1 part of iodine, 1 of potassium iodide, and 100 parts of water. The gut can be left in the solution till required. According to Rovsing's method, the catgut is first treated with ether for 24 hours and is then left for four days in a 4 per cent. aqueous solution of silver nitrate. Then alcohol is added (3 vols.) and the catgut is kept in this solution till required. C. L.

Rassfeld, L. Bakteriologische Leichenblutuntersuchungen mit besonderer Berücksichtigung der obligaten Anaerobier. [**The bacteriological examination of the blood of cadavera, with special reference to obligate anaerobes.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 393.

This paper deals with the bacterial content of the right ventricle of the heart in a series of 400 unselected autopsies. Cultivations were made aerobically and anaerobically. 50 per cent. of all the cases showed no bacteria. Aerobes and anaerobes alone or associated were found in the remainder. W. B.

Eggers, H. Experimentelle Beiträge zur Kritik der Kupferbehandlung der Tuberkulose. [**An experimental contribution to the criticism of the copper treatment of tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1921, **47**, 373–422.

Eggers's paper includes a searching criticism of the work of Gräfin von Linden, Strauss, and others, as well as a report of extensive investigations conducted by himself and Professor Ricker into the action of copper on tuberculosis. These investigations were carried out on rabbits, which were inoculated with tubercle bacilli of both bovine and human types. The tuberculous lesions provoked were both deep-seated (intraperitoneal) and cutaneous. The conclusions arrived at are not flattering to copper as a therapeutic agent in tuberculosis. Its direct local action on cutaneous tuberculosis is given due credit, but the subcutaneous injection of the chloride of copper in the treatment of internal tuberculosis was of little or no benefit. It is suggested that in the case of the skin the sloughing off of necrotic tuberculous tissue may be easily effected by the local application of copper ointment with resultant benefit; such a process in the deeper structures is a very different matter and is apt to be injurious. Even in the case of tuberculosis of the skin it was found that the penetrative action of copper was very limited, and acid-fast rods were demonstrable immediately below the thin, newly-formed epidermis. C. L.

Limousin, H. L'isolement des bacilles de Koch à partir des crachats tuberculeux d'après la méthode de Pétrof. [**Petrof's method of isolating tubercle bacilli from tuberculous sputa.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 558.

The author has applied the method of Petrof to a number of specimens of tuberculous sputum and isolated pure cultures of tubercle bacilli from all. The exact method of preparing the sputum for inoculation and the egg medium of Petrof are described. W. B.

Fontana, A. Contributo allo studio del virus dell' Herpes febrilis e progenitalis. [**Contribution to the study of the virus of herpes febrilis and progenitalis.**] *Pathologica*, 1921, **13**, 321 and 406.

(1) The inoculation, into the cornea of rabbits, of fluid obtained from vesicles of herpes febrilis and progenitalis was constantly followed by a keratitis either of the simple herpetic type or with characteristics simulating a parenchymatous form. No micro-organism was found in the sections of a cornea thus affected. The inoculation of a fragment of such a cornea into the anterior chamber of the eye of another rabbit was attended by negative results.

(2) In his second note on the subject the author explains that the apparent parenchymatous keratitis consisted of a herpetic lesion surrounded by a zone of infiltration leading to the formation of a superficial pannus. He also adds that, two or three days after inoculation, all the rabbits showed an increase in the body-temperature up to 41·5° C. In his experiments an encephalitic complication did not occur. The corneal re-inoculation of rabbits, which had recovered from the primary keratitis, was sometimes followed by an intense conjunctivitis lasting from four to six days. C. d. F.

Urizio, L. Di un reperto di corpuscoli nell' encefalo dei dermotifosi. [**Minute bodies in the brain from cases of typhus.**] *Pathologica*, 1921, **13**, 421.

Reference has already been made to Ficai's investigations (*Medical Science*, 1921, **5**, 157) on minute bodies found in the epithelial cells of the gastric mucous membrane of lice and in the nervous system from cases of typhus. Urizio now points out that such bodies may really be seen within the nerve-cells of specimens stained with Giemsa's fluid, Ehrlich's triacid mixture, and Pappenheim's pyronin methyl-green solution, but that they do not stain by Pappenheim's panchrom and Unna's haemalum and safranin method. In addition, Ficai's bodies are too large to be Rickettsia, and too simple in structure to be considered as conglomerations of the same. The fact that they were detected in the gastric mucous membrane of lice found on typhus patients has, according to Urizio, little importance, since similar granular inclusions appear to exist in normal animals and in the same situation. In conclusion, the author suggests considering Ficai's bodies as non-parasitic degenerative products, perhaps connected with the histopathology of the disease. C. d. F.

Kling, C., Davide, H., Liljenquist, F. Sjukdomsalstrarens förekomst i cerebro-spinal-vätskan vid encephalitis lethargica. [**Occurrence of the germ of lethargic encephalitis in the cerebrospinal fluid.**] *Hygeia*, 1921, **83**, 566–72.

On June 5, 1921, a woman of 40 developed clinically typical lethargic encephalitis. On the 7th, cerebrospinal fluid was withdrawn by lumbar puncture. On the 10th it was introduced by intracerebral injection into four rabbits, each of which received 0·2 c.cm. of the perfectly clear fluid, which yielded no growth on ascites-agar plates. During the next fourteen days there was no change of temperature nor sign of cerebral disease. On July 18 the animals still seemed perfectly well; two were killed on this date, and two a couple of days later. Macroscopically the brain seemed in every case perfectly normal. The microscopic examination was also negative in two cases, but in the remaining two the pia mater showed infiltration with mononuclear cells which were distributed in patches around the blood-vessels. In the substance of the brain similar perivascular infiltration was found, as well as comparatively large accumulations of mononuclear cells. Some of the blood-vessels of the brain were plugged with a hyaline substance and numerous leucocytes. A few ganglion cells showed degenerative changes. Cultivation of the brain substance under aerobic and anaerobic conditions revealed no bacteria, and direct examination for bacteria was also negative. These negative findings suggested that the microscopic changes in the brain and meninges were not due to an ordinary bacterial invasion but to the specific virus of lethargic encephalitis. The authors reproduce four microphotographs in support of their claim that the changes found in the experimental animals coincided exactly with those found in human beings dying of lethargic encephalitis.

As the disease had run such a hidden and uneventful course in the rabbits, it was anticipated that the virus might have died out before the animals were killed. This anticipation proved incorrect. On July 29 brain substance from the first series of rabbits was introduced by intracerebral injection into a second series of five rabbits. On August 23 two of these were killed, and in both cases the brain showed the microscopic changes characteristic of lethargic encephalitis. As the authors have found that rabbits are very resistant to this virus, they recommend the inoculation of several animals at a time, and they point out that though their procedure may ensure a correct laboratory diagnosis *intra vitam*, negative results are not necessarily reliable enough to exclude with certainty the diagnosis of encephalitis. C. L.

TRUFFI, M. Un caso di favo della cute glabra dovuto all' achorion α di Quincke. [**Case of tinea favosa of the hairless skin due to the achorion** α **of Quincke.**] *Pathologica*, 1921, **13**, 255.

Cases of favus due to hyphomycetes differing from the classical *Achorion schoenleinii* are rather rare. The species of such hyphomycetes described up to the present are: (1) *A. quinckeanum*; (2) *A. gypseum*; (3) *A. violaceum*; (4) *A. gallinae*; (5) *Oospora canina.* Truffi has had the opportunity of observing a case of tinea favosa limited to a small area of the skin of the back and certainly due to *A. quinckeanum.* This appears to be the second observation of the sort made in Italy, the first one having been published by Ingianni (*Boll. d. r. Accad. med. di Genova*, 1893). It is worth noting that in Truffi's case the infection appears to have been transmitted to the patient (a boy of 15 years of age) from a chicken which he kept in his home and which suffered from 'whitish crusts round the eyes and on the underlying skin'. C. d. F.

LEVADITI, C., MARIE, A., et **NICOLAU, S.** Virulence pour l'homme de la spirillose spontanée du lapin. [**Virulence of the spontaneous spirochaetosis of the rabbit to man.**] *Compt. rend. Acad. d. Sc.*, 1921, **172**, 1542.

The spontaneous spirochaetosis of rabbits and its resemblance to syphilis have recently been the subject of several communications from workers in various countries. The present authors have tried to determine whether the spirochaete in question (*Sp. cuniculi*, Jacobstal) is virulent for man or can protect against a subsequent infection with *Treponema pallidum.* Two of them (L. and N.) inoculated themselves on the arm after scarification with *Sp. cuniculi* and at the same time injected the same organism into a monkey (*Macacus cynomolgus*) and into a rabbit. No local or general lesion developed except in the rabbit, which showed the typical lesions of the disease. The Wassermann reaction of the subjects of the experiment was negative before the inoculation and remained so afterwards.

The authors conclude that *Sp. cuniculi* is not pathogenic to man and monkeys. The monkey has since been inoculated with *Treponema pallidum* in order to see whether he has been rendered immune to syphilis by his previous inoculation with *Sp. cuniculi.* The result of this second experiment has not been reported yet. J. R. P.

Thaysen, T. E. Hess. Positiv Wassermann-Aktiv Syfilis. [**Positive Wassermann reaction-active syphilis.**] *Ugesk. f. Læger.*, 1921, **83**, 759; 785.

Hess Thaysen criticizes as an easy but unwarrantable assumption that a positive W. reaction is indicative of active syphilis. A comparison of the W. R. and clinical records of 283 cases of syphilis showed that the severity of the manifestations bore no constant relation to the strength of the W. reaction. Discussing the criteria, apart from the W. reaction, by which to decide whether syphilis is active, latent, or cured, Thaysen admits that, as in the case of tuberculosis, it is very difficult to find direct and convincing evidence. He adduces the following, more or less circumstantial, evidence in support of his hypothesis that the W. reaction is positive in many cases in the 'latent stage' (with infection dating back at least four years), and is yet not indicative of an inevitable recurrence of clinical symptoms. Three series of wholesale W. tests of hospital patients in Denmark showed that, among 2,598 such patients, there were 57, or between 2 and 3 per cent., who gave a positive reaction without any history of infection or clinical sign of syphilis. These investigations showed that, if patients with a positive W. reaction and no other evidence of syphilis be assumed to be syphilitic, they represent one-fourth to one-fifth of all the cases of syphilis in a mixed hospital clientele.

Among 120 cases of syphilis Thaysen found only 46 with clinical signs of syphilis; among the remaining 74 there were 59 with a positive W. reaction. In other words, in the stage of 'late latency', the W. reaction is positive in about 50 per cent. With regard to the 57 cases referred to as showing a positive W. reaction and no other sign of syphilis, Thaysen calculates that, if the average age at the time of infection be assumed to be 25 years, then in 12 of these cases the disease must have been latent for 40 years or more, and in 21 for 20 years or more. According to Naunyn, 50 per cent. of the cases of cerebrospinal syphilis develop within the first 5 years after infection, and only about 2 per cent. as late as 20 years after infection. Syphilitic diseases of the aorta give rise to symptoms about 20 to 22 years after infection (Romberg and Denecke). In view of such evidence, Thaysen argues that in most of the above 57 cases it is probable that the syphilis will continue to remain latent, notably in the 28 whose infection had probably occurred more than 25 years earlier. He also argues from his statistics that the number of patients with a positive reaction and latent disease is considerably greater than was once thought, and that the combination of a positive W. reaction with 'late latency' is to be found in somewhat less than half of all the cases of syphilis surviving infection by 10 to 20 years. The conclusion is drawn that, if a patient survives 25 years after infection, and if during most of this period there has been no clinical evidence of active syphilis, the disease will, in most instances, remain clinically inactive even if the W. reaction be positive.

C. L.

Christiansen, J. Negativ W.R.-aktiv Syfilis. [**Negative Wassermann reaction; active syphilis.**] *Hosp.-Tid.*, 1921, **64**, 315–19.

This paper is a study of the cases of syphilis treated at the Rudolph Berghs Hospital in 1918–20, in which Wassermann's reaction was negative in spite of clinical evidence of an outbreak of secondary or tertiary syphilis. In this 3-year period 1663 cases of syphilis were examined, and of 12 patients who had never received specific treatment, and who yet gave a positive reaction in the second or third stage of the disease, as many as 7 were either pregnant or were still in the puerperium. No explanation to account for this curious finding is offered. C. L.

Stura, G. Una modificazione al metodo Fontana per la colorazione della spirocheta. [**Modification of Fontana's method for the demonstration of *Spirochaeta pallida*.**] *Pathologica*, 1921, **13**, 98.

This modification concerns the staining stage of Fontana's method and should be carried out as follows: (1) Smears fixed by heat are kept for a few minutes in a solution consisting of formalin 50 c.cm., acetic acid 2 c.cm., distilled water 150 c.cm. (2) After washing with distilled water, pour on the slide a few drops of a mixture of 5 gr. of tannic acid, 3 gr. of carbolic acid, and 100 c.cm. of distilled water. Warm on a flame up to boiling-point. (3) Wash repeatedly. Pour on the slide pure ammonia; after a few seconds pour it off, and, without washing, allow a 0·5 per cent. solution of $AgNO_3$ to pass from one side of the slide over the smear. As soon as this has become brown the staining is finished and there only remains washing the preparation and drying it over a flame. C. d. F.

Sangiorgi, G., e Fontana, A. Ulteriori ricerche sugli spironemi dei condilomi acuminati. [**Further investigations on spironemata of pointed condylomata.**] *Pathologica*, 1921, **13**, 218.

Reference has already been made to the investigations of the two authors on the same subject (*Medical Science*, 1921, **4**, 158). They now communicate that attempts at cultivating in peptone-water their spironema type B have failed. Further investigations on material from other cases of pointed condylomata have shown the presence of deformed and swollen spironemata which, however, do not differ essentially from those previously described. C. d. F.

Fontana, A. Reperti spirocheti-simili nella psoriasi volgare. [**Spirochaeta-like appearances in psoriasis.**] *Pathologica*, 1921, **13**, 259.

Quite recently Rask (Christiania, November 1920, *Policlin.*, 1920, *sez. pr.*, **28**, 272) has observed in the patches and blood of psoriatics a spirochaeta considered by him as the cause of the disease (*Spirochaeta sporogena psoriasis*). Before him Prowazeck stated that he had found, in two patients, small elements of the spironema type weakly stainable by Giemsa's method and provided with thin terminal hairlets. Fontana has tried to control the truth of such findings. The investigation of the blood and of sections of skin patches of psoriatics was attended by negative results. In smears made from the same patches and stained by the Fontana-Tribondeau method, many thread-like twisted forms were seen. But these appearances increased in number the greater was the amount of corium comprised in the skin fragments, and similar results were obtained from patients affected by other skin diseases. Hence the suggestion that Prowazeck and Rask may have made some mistake, possibly owing to an increased colorability, under pathological conditions, of certain fibrous elements of the skin. C. d F.

Holker, J. The viscosity of syphilitic serum. *J. Path. & Bacteriol.*, 1921, **24**, 413.

By means of a viscosimeter invented by himself the author has studied the viscosity of syphilitic sera under varying conditions, and finds that it is increased when the serum is inactivated at 55° C. for 20 minutes. Prolonged standing of sera at 56° C. increases the viscosity of sera of syphilitics treated or untreated, negative or positive, more readily than that of normal persons with a negative W.R. The viscosity-concentration curve indicates that on diluting serum with normal salt solution some of the 'soluble' viscous form of protein is converted into the 'insoluble' non-viscous form with a consequent relative reduction in viscosity. The serum of untreated syphilitics tends to be more viscous than that of normal persons, this being more marked in the secondary and still more in the tertiary stage of the diseases. In 'parasyphilis' it is, however, not so marked. W. B.

Ponder, E. The occurrence of haemolytic substances in normal urine. *Brit. J. Exper. Pathol.*, 1921, **2**, 192.

Sixty-four per cent. of normal unselected urines were found to be haemolytic. If the non-haemolytic specimens had been examined repeatedly they would probably have been found to be haemolytic at some time. It seems that the presence of haemolytic action is more frequent in insanity, but in itself is not abnormal. P. F.

Yorke, W., and **Macfie, J. W. S. The mechanism of autolysis in paroxysmal haemoglobinuria.** *Brit. J. Exper. Pathol.*, 1921, **2**, 115.

When the blood of a case of paroxysmal haemoglobinuria was cooled at 0° C. for 5 minutes only, before warming at 37° C. for 1 hour, the amount of haemolysis which resulted was about 10 times as great as that which occurred when the cooling was prolonged for 30 minutes. The explanation of this depends on the facts that in haemoglobinuric serum immune body is greatly in excess of complement, and that sensitized red cells take up the mid-piece of the complement at 0° C, whereas the persensitized erythrocytes can only absorb end-piece at higher temperatures. Many more erythrocytes are sensitized after cooling for 30 minutes than for 5 minutes; consequently mid-piece is diffused amongst a correspondingly greater number of sensitized erythrocytes. On warming, the concentration of end-piece available for each persensitized erythrocyte depends directly on the number of these, and when the number is very great (e. g. after cooling 30 minutes) the concentration is insufficient to produce lysis. The immune body-erythrocyte reaction is reversible, but ceases to be so as soon as the erythrocytes have become persensitized. Experiments conducted with the object of determining whether the immune body is thermostable or thermolabile were inconclusive.

P. F.

Evans, C. L. The reaction of the blood in secondary anaemia. *Brit. J. Exper. Pathol.*, 1921, **2**, 105.

Although the immediate effect of haemorrhage is a lowering of the alkali reserve of the blood, the response of the respiratory centres may partially compensate, or even over-compensate, for this change, so that the circulating blood may be either more acid, or less acid, or of the same reaction even, after as before the haemorrhage. After twelve hours the reduction in alkali reserve is compensated, owing to increased excretion of acid by the kidney; subsequently the alkali reserve of the blood may become higher than the normal and remain at this level until the corpuscular degeneration is complete. The response is a protective one against acidosis.

P. F.

del Rio-Hortega, P., y **de Asua, F. J.** Sobre la fagocitosis en tumores y en otros proceses patológicos. [**On phagocytosis in tumours and other morbid processes.**] *Arch. Cardiol. y Hematol.*, 1921, **2**, 161–220.

In a long and important paper on phagocytosis Rio-Hortega and Asua reach the following conclusions: (1) In all sorts of tumours, in acute and chronic inflammatory processes, specific or otherwise, in the normal or pathological lymphoid tissues, and in morbid states of other organs, there exist varying evidences of phagocytic activity. (2) The phagocytic cells are identical with the macrophages of Metchnikoff and stand out well when stained with ammoniacal carbonate of silver. (3) The number of macrophages is in proportion to the amount of connective tissue and the presence of haemorrhages or necrosis of tissues. (4) The morphology of the macrophages is very variable and may alter according to the class of cell in which they originate, the movements of their protoplasm, the density of the structure in which they are placed, and their content of cells, &c. (5) At least six more or less definite forms can be distinguished, namely, globular, amoeboid, branched, flat, elongated, and sponge-like. (6) The structure of the macrophages may appear homogeneous, granular, or vacuolated. (7) The shape, size, and position of the nucleus varies with that of the cell according to the environment. (8) The fact that too long staining with silver prevents the selective staining of the macrophages suggests the possibility that these cells contain a ferment forming with the silver a compound which is soluble in excess of the reagent. (9) Macrophages may originate in various cells, e. g. undifferentiated embryonal cells, fibroblasts, cells of the connective tissue, and even detached endothelial cells. In cases of internal haemorrhages it appears that the large mononuclears of the blood act as macrophages. (10) No formation of macrophages from fat-cells has been seen, nor h diapedesis of large mononuclears or of endothelial cells been detected. (Macrophages may revert to primitive cell types.

G. W

MACKENZIE, G. M. Serum desensitization. *J. Am. M. Ass.*, 1921, **76**, 1563.

Mackenzie advises the following procedure for the purpose of desensitizing those who are susceptible to horse-serum, which is a common constituent of such therapeutic sera as may have to be used for diphtheria, &c., in those who have perhaps been sensitized by previous injections of antitetanic or other sera. Not more than 0·025 c.cm. should be given subcutaneously and the amount doubled every half-hour until 1 c.cm. has been given. Then 0·1 c.cm. is given intravenously and the dose doubled every twenty minutes until 25 c.cm. have been given. Four hours later 50 c.cm. may be given, and after eight hours treatment may be continued as desired. If any reaction occurs the last dose which gave no reaction should be repeated. All injections should be given slowly. Serum should never be injected without there being epinephrin solution close at hand. This same procedure should be employed in the desensitization of asthmatics, &c. G. W.

SCHNABEL, A. Zum Mechanismus der antihämolytischen Wirkung der Chinaalkaloide. **[The mechanism of the anti-haemolytic action of quinine alkaloids.]** *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **32** (Orig.), 153.

It is well known that a haemolytic system may be put out of action by a variety of substances which have been generally supposed to be anticomplementary or to act upon the amboceptor. Quinine and optochin produce such a result. Working with a haemolytic system consisting of sheep corpuscles, rabbit amboceptor, and guinea-pig complement, the author shows that the delayed haemolysis in the presence of quinine or optochin solutions is due to the fact that these alkaloids are taken up and then given off by the red blood corpuscles. W. B.

VAN HERWERDEN, M. A. A simple method of counting blood platelets. *J. Am. M. Ass.*, 1921, **76**, 723.

Van Herwerden uses a diluting fluid composed of 10 per cent. urea solution in water and 0·9 per cent. NaCl in the proportions of 21 to 9. The finger is pricked and the first drop of blood wiped away. The pipette is filled to the 0·6 mark and allowed to empty down to the 0·4 mark on to the wound. A drop of blood is squeezed out into the fluid. The mixed blood and diluting fluid is drawn up to the 1 mark and the platelets may be counted in the ordinary haemocytometer after thirty minutes. The red corpuscles are destroyed by the urea whereas the platelets are preserved and their agglutination prevented.

The author finds the normal figures to vary between 326,000 and 217,000, per c.mm. G. W.

DELCOURT-BERNARD, E. État actuel de nos connaissances sur la nature et le rôle des plaquettes sanguines. **[The present state of our knowledge as to the nature and function of blood platelets.]** *Arch. méd. belges*, 1921, **74**, 210–19.

Delcourt-Bernard sets forth the three following facts as the most portant of those definitely ascertained about the platelets. First, these independent elements of the blood reacting at once, and always in the ne way, to the presence of any foreign body in the blood-stream. Secondly,

by their action, physico-pathologic or micro-chemical, they act as phagocytes, preparing the invader for the attentions of the polymorphs to which they presently give place. Thirdly, the agglutination of platelets and of micro-organisms have much in common but are probably distinct processes.
G. W.

Savini, E. Sur les lipoïdes des leucocytes. [**The lipoids of leucocytes.**] *Arch. méd. belges*, 1921, **74**, 325–9.

Savini has stained leucocytes with Scharlach R after a preliminary treatment with 5 per cent. copper bichromate. He thinks that the bichromate is not a mordant but acts by decreasing the solubility of the lipoids, of which he finds evidence in practically all the cells of the blood in varying degrees. These are not due to recent digestion of lipoid-containing substances, but are an essential part of the structure of the cells.
G. W.

Barcroft, J. Haemoglobin. *Lancet*, 1921, ii, 46.

Barcroft points out that a solution of haemoglobin in water and a suspension of the same amount in the corpuscles of a similar bulk of blood have very different properties. The haemoglobin solution is more viscous and would require a stronger heart force, it would lose haemoglobin through the kidney filtering membranes, it would be very susceptible to every change of reaction, &c., of the serum, and finally it would not be so equally oxygenated or reduced as the red cell haemoglobin is. Barcroft thinks that these considerations have not often received the attention which is their due.
G. W.

Goyanes, J. Estudio clínico sobre la trombosis. [**Clinical study of thrombosis.**] *Arch. Cardiol. y Hematol.*, 1921, **2**, 5.

Goyanes sets forth the different recognized varieties of thrombosis, grouping them as hyaline, white and red according to the nature of the clot and also according to their aetiology. His attention has been given chiefly to the post-partum clots, and these he considers due to a concatenation of favourable circumstances, namely, anaemia, stasis, and the physiological thrombosis of the placental site. G. W.

Householder, R. Enlargement of the spleen in experimental acidosis. *J. Am. M. Ass.*, 1921, **76**, 1556.

Householder has injected hydrochloric acid subcutaneously into guinea-pigs and thereby produced a condition of acidosis demonstrable by a decreased ability of the plasma to combine with carbon dioxide. Therewith he has noted the development of anaemia and splenomegaly. G. W.

Pagniez, Ph. De la sédimentation des globules rouges du sang. [**The sedimentation of red blood corpuscles.**] *Presse méd.*, 1921, **29**, 405.

Pagniez reviews the work of several authors on the quick sedimentation of the red cells in pregnant women and co-relates therewith the observation that anaphylactic shock cannot be produced in pregnant animals. He assumes that this is due to some alteration in the colloidal state and suggests that the sedimentation may depend on the same factors. There is no doubt that if we could control whatever factors are in question we should be able to do much for those who suffer from asthma, &c., except only during pregnancy. G. W.

Bermejillo, M. Anhidre carbonico y viscosidad sanguinea. [**Carbon dioxide and the viscosity of the blood.**] *Arch. Cardiol. y Hematol.*, 1921, **2**, 54.

Bermejillo reviews experiments on the causes of increased blood viscosity and concludes that increase of CO_2 is an important factor and that it is responsible for an actual increase in size of the red cells. G. W.

Van den Bergh, A.-A. H. La recherche de la bilirubine dans le plasma sanguin. [**Bilirubin in the blood plasma.**] *Presse méd.*, 1921, **29**, 441.

Van den Bergh brings forward an improvement on Gilbert's method of estimating the bilirubin of the plasma. The method depends on the fact that bilirubin gives a diazo reaction which is not interfered with or given by other constituents of the blood. His qualitative test is as follows. One volume of serum is mixed with two of 96 per cent. alcohol and the precipitate removed by centrifugalization. To one volume of the resulting clear fluid is added one-quarter of the amount of diazo solution, which should be freshly prepared. If even so little as 1 in 1,500,000 of bilirubin is present the characteristic play of colours appears. Half a centimetre of serum is sufficient for this test. Should the addition of the diazo solution produce some opacity due to separation of fatty materials taken up by the alcohol, this can be neutralized by heating or by the addition of a few drops of ether. To make a quantitative estimation nothing is wanting except a standard which shall be sufficiently constant. The author has found it very laborious to make a standard solution by means of bilirubin solutions of known strength, but has fortunately hit on a stable solution which gives the appropriate colour. This is composed of sulphocyanide of iron in ether. 1/32,000 of this is exactly equivalent in colour to 1/200,000 of bilirubin-diazo solution. Details of the preparation of all solutions are given. There are two errors in this method. The first is the personal error, and this can only be eliminated by practice. The second is due to the fact that in a serum rich in bilirubin some of this substance is carried down by the precipitate of albumins which follows the addition of alcohol.

In the application of these reactions to clinical problems van den Bergh has discovered certain other points of interest. In many cases the reaction is in no way interfered with if water be used instead of alcohol in the primary dilution of the serum. This is so in the serum of cases of bile retention from obstruction to the bile passages. But in those suffering from haemolytic icterus or pernicious anaemia the reaction is delayed or incomplete if water be used, but promptly appears if alcohol be added to the extent of two volumes (of the bilirubin-diazo mixture?). The former action van den Bergh speaks of as 'immediate' and the latter he calls 'delayed'. He is inclined to believe that the action of the alcohol in hastening delayed reactions is due to the breaking of some bond otherwise subsisting between the bilirubin and blood albumins, which of course remain in watery solutions. It is obvious that the two types of reaction must be due to some difference in powers, composition or potentialities of two sorts of bilirubin. That two varieties occur is suggested by the way in which the diazo reaction is apt to develop speedily up to a point and then to complete its colour change more slowly—the diphasic reaction of Feigl. These two further differ in that the bilirubin of the immediate reaction is attacked more readily by oxidizing agents than the other and is much more easily precipitated with the albumins. Of further interesting facts deduced from experiments with van den Bergh's method may be noted that the stains of bruises give undoubted evidence of bilirubin and that the blood in the splenic vein in pernicious anaemia and other haemolytic diseases contains more bilirubin than serum from other parts of the body. G. W.

Ecker, E. E., and **Goldblatt, H. Thyroidectomy and parathyroidectomy with relation to the development of immune substances.** [**B.**] *J. Exper. M.*, 1921, **34**, 275.

The authors have carried out an investigation to determine whether and to what extent thyroidectomy and parathyroidectomy influence the course of immunization and the production of antibodies, especially haemolysins produced by the injection of sheep corpuscles. The results are set out in a series of curves from which it is concluded that after thyroidectomy with partial parathyroidectomy the maximum and average haemolytic titres of the sera of rabbits injected with sheep erythrocytes are equal to or higher than those of control animals. The operation does not cause serious disturbance in the animal. If, however, complete thyro-parathyroidectomy is carried out, only a small proportion of the animals survive, and such survivors develop haemolysins of uniformly low titre towards sheep or ox corpuscles. W. B.

BIOCHEMISTRY

Dutcher, R. H., and **Wilkins, S. D. Vitamin studies. VII. The influence of fresh alfalfa upon the weight of testes in single comb white Leghorn cockerels.** *Am. J. Physiol.*, 1921, **57**, 437.

The observations were carried out to study the effects of vitamins upon poultry feeding, particularly the influence of dietetic deficiencies upon the reproductive organs in poultry.

The testes of White Leghorn cockerels did not develop on a diet of polished rice. The atrophy could be prevented by the addition of green alfalfa.

Atrophy of the testes was obtained in cockerels which had actually increased in body-weight, indicating that atrophy of organs is not due necessarily to general inanition and loss of body-weight. W. C.

Cowgill, G. R. A contribution to the study of the relation between vitamin-B and the nutrition of the dog. *Am. J. Physiol.*, 1921, **57**, 395.

The author confirms the observations of Karr that in dogs the withholding of the water-soluble vitamin B leads to a greatly diminished intake of food. The same has been observed in rats by Hopkins and by Drummond. The dogs eventually developed polyneuritis and vomiting. Alcoholic extracts of wheat embryo, navy bean, and rice polishing contain water-soluble vitamin B. W. C.

Abderhalden, E., u. **Wertheimer, E. (VII), Abderhalden, E. (VIII).** Weitere Beiträge zur Kenntnis von organischen Nahrungsstoffen mit spezifischer Wirkung, VII. VIII. [**Further contributions to our knowledge of organic food-components having specific effects.**] *Arch. f. d. ges. Physiol.*, 1921, **191**, 258, 278.

VII. Extracts of yeast or bran increase the gaseous metabolism of various tissues (well known). Casting round for other substances that do the same thing the authors get positive results with glutamine, glutaminic acid, pyrrolidine-carboxylic acid, tryptophane, rape-oil, cod-liver oil, valerianic, formic, tartaric, citric, oxybutyric, oxyisocaproic, lactic, pyric, acids, hexose phosphate, glycero-phosphate, arsenites, and various antiscorbutic juices. Yeast extract also accelerated plant respiration. The effect of light on the respiration of human blood is nil; if eosin is added, diffuse light accelerates and bright light inhibits respiration. VIII. Guinea-pigs fed on scorbutic diets had a lowered gaseous exchange, which was raised by yeast administration. Administration of cystine or of peptone from feather, hair, or guinea-pig skin hydrolysis, did not affect the growth of hair.

C. L. E.

Adler, L. Untersuchungen über die Funktion des Pankreas. [**Investigations on pancreatic function.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **91**, 110.

Extract of thyroid gland injected into a hibernating hedgehog results in a stimulation of metabolism, a rise in body-temperature, and the waking of the animal. Extract of thymus and adrenalin have the same action, while pancreatic extract is inactive. Moreover, if pancreatic extract prepared from one hibernating hedgehog be injected into another the subsequent effect of thyroid injection is inhibited. Similarly, the effect of thymus extract and the effect of adrenalin are both inhibited by previous administration of pancreatic extract, but the inhibition of the adrenalin action is less than that of the action of thymus extract. J. H. B.

Paulesco. Action de l'extrait pancréatique injecté dans le sang. [**Action of pancreatic extract injected into the blood.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 555. (*Physiol. Abstr.*, 1921, **6**, 442.)

This author now claims to have shown what has so long been in doubt, that pancreatic extract injected into the blood of a de-pancreatized dog diminishes the hyperglycaemia and glycosuria, and also the acetone bodies in blood and urine. The effect is at its maximum in two hours, and lasts as long as twelve hours. The more extract is given, the greater the effect. Extract given to a normal dog diminishes the blood-sugar. J. H. B.

King, J. L. A study of the anticoagulating substances in the mucous membrane of the uterus. *Am. J. Physiol.*, 1921, **57**, 444.

This paper deals with the problem of the non-coagulability of the menstrual blood. Of the various explanations which have been given one is that the uterine mucosa contains an anticoagulant. This view was tested in the present paper by experiments with press-juice and saline extracts of the uterine mucous membrane from the pig. The results do not support the idea mentioned above. From an examination of menstrual blood the author arrives at the conclusion that the non-coagulability of menstrual blood is a myth, and that the menstrual discharge consists of serum with small bits of disintegrated clot. The so-called 'menstrual blood' contains neither fibrinogen, thrombin, nor antithrombin. It is suggested that the blood clots as it leaves the vessels of the mucosa, but locally and in small amounts, so that no large mass of fibrin is formed, and only small fragments of clot, more or less disintegrated, pass from the uterus. W. C.

Myers, V. C., and **Short, J. J.** **The potassium content of normal and pathological human bloods.** *J. Biol. Chem.*, 1921, **48**, 83.

This paper deals with a suggestion of Smillie, that in nephritis potassium salts were readily absorbed, but not easily excreted. In this way an injurious concentration in the blood was reached. The idea was based upon the observation that the administration of potassium salts to cases of nephritis leads to poisoning. A similar effect was noted in experimental uranium nephritis.

Myers and Short were unable to find an increased content of potassium in either the serum or the whole blood of seven nephritic patients. The potassium content of the whole blood was on the contrary diminished. The theory of Smillie is therefore not supported by their experiments.

R. A. P.

Bornstein, A., and **Vogel, R.** Parasympathicusgifte und Blutzucker. [**Parasympathetic poisons and the blood sugar.**] *Biochem. Ztschr.*, 1921, **122**, 274.

An injection of pilocarpine or of physostigmine, choline or acetyl choline, leads to a stimulation of the parasympathetic with a rise in the sugar in the blood in the normal dog. This type of hyperglycaemia is found to be prevented or slowed by a previous injection of atropine. Following this line of thought, they have been led to test the effect of atropine doses upon diabetics. In some cases (though not in all) it was found that an injection of atropine was followed clinically by a reduction in the amount of sugar in the blood. From this it is concluded that in the diabetic complex of symptoms in some cases, at least, there is a nervous factor involved.

R. A. P.

Barbour, H. G., and **Herrmann, J. B.** **The relation of the dextrose and water content of the blood to antipyretic drug action.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 165.

It is known that glucose has an antipyretic action, which appears to be connected with the dilution of the blood following its administration. In the present paper the authors have studied the blood concentration and sugar content of the blood of normal animals and those which have been made febrile by the injection of a *B. coli* vaccine. During the period of pyrexia certain antipyretics—sodium salicylate, antipyrine, aspirin, and quinine were given. It was found that all these drugs increase the blood-sugar concentration. In the febrile animals the blood is diluted. They conclude that the mobilization of dextrose is one of the chief factors responsible for the blood dilution by antipyretic drugs in fever.

C. G. L. W.

Barbour, H. G., and **Freedman, B. P.** **Effects of pilocarpine upon salivary secretion in normal and febrile dogs.** *Am. J. Physiol.*, 1921, **57**, 387.

In two dogs salivary response to pilocarpine became diminished during the height of coli fever. The authors associate this phenomenon with the increased concentration of the blood which in previous observations they had found to occur in fever. They hold that the diminished secretion is due to lack of available water rather than to a pustulated cloudy swelling of the gland cells. In one of the two dogs the diminished response to pilocarpine persisted on the day following the fever when the temperature had become normal. No actual estimations of the concentration of the blood were carried out in these two dogs. In one dog the concentration in the saliva of the total solids and the inorganic salts was estimated. The concentration of the inorganic salts was distinctly diminished on the day of fever, the concentration of the total solids showed a slight increase on that day. It is not explained how these findings fit in with the theory of lack of available water in the blood. W. C.

Kühlewein, M. v. Cholin als Hormon der Darmbewegung. V. Experimentelle Therapie der Magen-Darmlähmung nach Chloroformnarkose. [**Choline as a peristaltic hormone. V. Gastro-intestinal paralysis after chloroform narcosis.**] *Arch. f. d. ges. Physiol.*, 1921, **191**, 99.

Gastro-intestinal stasis after 2 hours of deep chloroform anaesthesia was demonstrated in cats by the X-ray method: the absolute stasis lasted for 2 hours and was followed by impaired motility for 20 hours. Intravenous injection of 0·005—·015 gm. per kg. of choline—HCl overcame the stasis and also stimulated the large intestine; if slowly injected there was no harmful effect. The stasis following $CHCl_3$ does not appear to be due to loss of choline, but rather to paralysis of the Auerbach plexus; at all events, dialysates from the intestines of normal and chloroformed cats, whether used direct or acetylated, had quantitatively similar effects on rabbit's bowel. C. L. E.

Barbour, H. G., and **Hjort, A. M.** **Notes on the toxic effects of chlorine antiseptics in dogs.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 201.

Given intraperitoneally, chloramine T. appears to possess one and one-half times the toxicity of Dakin's solution and but one-fifth the toxicity of corrosive sublimate. All three of these antiseptics can produce acute or chronic peritonitis. They produce circulatory and muscular collapse with reduction in body temperature. C. G. L. W.

Myers, V. C., and **Killian, J. A.** **Studies on the influence of phenyl cinchoninic acid and the methyl ester of paramethylcinchoninic acid on renal excretion.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 213.

The authors have studied the effect on the kidney of the two substances which are better known as atophan and novatophan. It has been shown by certain experiments that substances of this class not only sweep out the uric acid from the blood but lower the urea and non-protein nitrogen content of the fluid. Denis has suggested that the beneficial effect of sodium salicylate may be due in part to the increased excretion of toxic products in this way. Atophan and novatophan were given by Myers and Killian to cases with derangement of the kidneys. The blood was examined for uric acid, urea, creatinine, and chlorides. In almost all cases there was a diminution in the content of these constituents of the blood. They conclude that atophan and novatophan exercise a general stimulant effect on kidney excretion. This is of course most marked for uric acid. C. G. L. W.

Kochmann, M. Wirkung des Cocains auf das Froschherz und seine Gewöhnung an das Gift. [**Action of cocaine on the frog's heart, and the accommodation to the poison.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 158.

Concentrations below 1/300,000 molar are ineffective; between 1/160,000 and 1/300,000 may slightly improve the amplitude of the beat; 1/20,000 – 1/100,000 causes slowing and reduction of amplitude; 1/20,000 – 1/2,000 first slow and weaken, and finally arrest the ventricle; while 1/2,000 solutions cause diastolic arrest, first of ventricle, then of auricle (1/1,000 molar = 0·034 per cent.). Partial accommodation to the more moderate strengths may occur, and complete recovery when the drug is replaced by pure Ringer. C. L. E.

Kolm, R., u. Pick, E. P. Über inverse Herzwirkungen parasympathischer Gifte. [**Reversed cardiac effects of parasympathetic drugs.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 108.

Acetyl-choline, muscarine, and pituitrin do not cause diastolic arrest in the isolated hearts of summer frogs perfused with a fluid rich in calcium; if there is a deficit of K they even cause contracture. Atropine does not affect the contracture caused by calcium-acetyl-choline, but ergotamine can prevent it. The contracture is therefore supposed to be due to a stimulation of sympathetic nerves rendered over-excitable by Ca; in other words, a latent sympathicotropic property of these 'vagal' drugs is revealed under these conditions. The acetyl-choline contracture does not take place after the application of an auriculo-ventricular ligature. C. L. E.

Vorschütz, J. Ruhestrom und Durchlässigkeit. II. Untersuchungen mit Alkaloidsalzen und einigen anderen organischen Elektrolyten. [**Electric rest currents and permeability. II. Investigations with alkaloid salts and some other organic electrolytes.**] *Arch. f. d. ges. Physiol.*, 1921, **190**, 54.

Experiments with alkaloids, in the form of their salts, gave no definite indications in favour of Beutner's theory, because those that were not definite muscle poisons produced little effect on the electrical state of the tissue. The effect of alkaloidal salts on muscle is due to the free base formed by hydrolysis. Other organic substances, such as the salts of quaternary ammonium bases, Na salts of salicylic, benzoic, and lower fatty acids, also produce effects which do not harmonize with Beutner's theory. C. L. E.

Macht, D. I., and Ting, G. C. **Response to drugs of excised bronchi from normal and diseased animals.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 111.

In the majority of instances the pharmacological action of drugs is determined with normal tissues. The authors point out that attention should be paid at the same time to the action on tissues which are pathological.

They compared the action of drugs on normal bronchi with that on bronchi which had been removed from animals (pigs) suffering from broncho-pneumonia due to various causes. The physiological response in the diseased bronchi was feeble, and in some cases entirely absent. C. G. L. W.

Hooper, C. W., Kolls, A. C., and Wright, D. Quantitative pathological studies with arsenic compounds. I. The influence of fasting and various diets on arsphenamine poisoning, and the comparative toxicity of arsphenamine, neo-arsphenamine, and para-oxy-meta amino-phenyl-arsenoxide. *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 133.

The authors have investigated the important point of the toxicity of arsphenamine (salvarsan) and neo-arsphenamine (neo-salvarsan) as influenced by the administration of food. They show that a diet of bread, rolled oats, and milk, given the previous day to albino rats, exercises a marked protective influence on the toxicity of the arsenic preparation. This corroborates other observations made in phosphorus, chloroform, and aceto-nitrile. The authors show that a carbohydrate diet gives much more efficient protection than a meat diet. The carbohydrate diet must be a mixed one, for feeding cane sugar alone lowered the resistance of the animals. A method is proposed for standardizing the animals on which toxicity tests are made, and emphasis is laid on the importance of the dietary history of these animals.

The administration of mercury does not materially increase the severity of the renal injury produced by arsphenamine. C. G. L. W.

Dale, H. H., and Dudley, H. W. The physiological action of N-methyl histamine and of tetrahydropyrido-3-4-iminazole (imidazolisopiperidin of Fränkel). *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 103.

Attempts have been made to correlate the action of the active principle of the pituitary with histamine. The authors have examined certain derivatives of histamine, more especially the imidazolisopiperidin of Fränkel.

None of these compounds have at all the same physiological activity on the uterus as histamine itself. C. G. L. W.

Rogers, F. T., and Wheat, S. D. Studies on the brain-stem. V. Carbon dioxide excretion after destruction of the optic thalamus and the reflex function of the thalamus in body temperature regulation. *Am. J. Physiol.*, 1921, **57**, 218.

Observations on pigeons. Removal of the cerebral hemispheres leaving the optic thalamus intact does not interfere with the normal temperature regulation. Destruction of the optic thalamus renders the animal poikilothermous. Reflex changes of muscle tone and of the sympathetic system, which are concerned in the regulation of the body temperature and are induced by stimulation of the temperature nerves of the skin, involve the thalamus as an essential part of the functional pathway. This is in confirmation of previous work by Isenschmid and Krehl, who, in rabbits, found that the parts of the thalamus necessary for temperature regulation were located in the posterior, central, and ventral grey regions. W. C.

RADIOLOGY

Radiotechnique

Preliminary Report of the X-ray and Radium Protection Committee, 1921.

This preliminary report is the first of its kind issuing from the above committee. In view of the dangers which exist in radiation work, unless adequate precautions are taken, and of the lack of uniformity existing at the present time in these measures of protection, this report is timely in its appearance. The standpoint taken is that the dangers at the present day of work with X-rays and radium are known and can be adequately guarded against by thorough and systematic precautions. These precautions are not only concerned with the protection of the body against penetrating types of radiation; the whole of the working conditions of the personnel are surveyed, attention being directed to the necessity (1) of adequate space and ventilation in radiological departments; (2) of appreciable off-duty and holiday periods to compensate for the hours necessarily spent in dark rooms; (3) of a strict adherence on the part of the personnel to the precautions recommended for their safety.

The report endeavours to lay down protective specifications for X-ray apparatus intended for different purposes. These requirements vary very considerably according to the degree of penetration of the rays. In view of the fact that so many different protective materials are used, the recommendations are all made on the basis of 'equivalent lead', and this should simplify in future any statements which are made as to the efficacy of protective materials.

In working with radium the dangers of manipulating large quantities of the emanation are considered as well as those due to the penetrating gamma-rays. The various radium institutes now adopt rigorous methods of avoiding these dangers, and institutions will be well advised to consider these precautions before undertaking work of this character on an extensive scale. The blood changes which have been observed in people who have suffered from over-exposure to radiation induce the committee to recommend that systematic blood counts of the personnel be made with a view to recognizing any such changes as soon as possible.

The committee adopts an attitude of caution regarding the possibility of still more rigorous measures of protection being necessary as the range of penetrating power of X-rays increases. The committee intends to pursue researches upon several of the questions which arise out of the dangers of irradiation and the methods of avoiding them. Copies of this Preliminary Report may be had on application to the Hon. Sec. X-ray and Radium Protection Committee, c/o Royal Society of Medicine, London. S. R.

BROCA, A. Rapport sur les dangers des radiations pénétrantes et les moyens de les éviter. [**A report on the dangers of penetrating radiations and the methods of avoiding them.**] *J. de radiol. et d'électrol.*, 1921, **5**, 414.

The author begins by giving an account of emanation in which he states that it is only dangerous when confined, and specially so to those charging the tubes: those who apply either radium or its emanation to patients do not come under the direct action of its rays because of the screens. He considers the question of the effect on the atmosphere and concludes that good ventilation will avert all danger. He puts forward the hypothesis that possibly the minute trace of emanation often observable in the air is useful to life or even indispensable, and says that institutes of radium should not be classed as unhealthy institutions with the quantities at present in existence.

Dangers of penetrating radiations for the manipulators—methods of protection. An account of the various lesions caused by X-rays and radium is given and the author states that in institutes of radium, lesions analogous to the chronic lesions caused by X-rays are seen; leucopenia especially is mentioned. To combat this the personnel at the Radium Institute of Paris have their blood examined periodically and are given the holidays necessary to maintain the blood in order; these precautions have been found to be sufficient. In brief, the points to be observed are: (1) only handle a radioactive tube with forceps, taking advantage of the falling off of the radiation according to the square of the distance; (2) to protect deep organs from effects at a remote date use lead screens.

Protection of medical personnel and their surroundings. The author states that every X-ray bulb should have an absorbent cover and every beam of rays should be as small as possible. These devices will not always be sufficient when using penetrating rays over a long period, and here advantage of the square of the distance law can be taken.

Reference is made to the ionization current due to the penetrating radiation of the atmosphere, which in the author's laboratory is 2×10^{-13} to 3×10^{-13} amps. and to the current caused by the discharge of a Coolidge tube 5·5 m. distant from the electroscope which is about 5×10^{-13} amps., i. e. a value often found in some natural atmospheres. With a standard of 9×10^{-5} gm. of radium a discharge of the electroscope is seen equal to that of the penetrating radiation of the atmosphere for a distance of 20 cm. It is sufficient then to warn the personnel not to stand continually by the patient's bed: 3 m. from the bed there is no danger.

Conclusions. The younger radiologists who take the precautions mentioned above are not affected by chronic radiodermatitis or by leucocytic disorders. At present a radiological installation is not prejudicial to the neighbourhood. In conclusion the author states that those who make radiology their work are much the same as those medical men who are daily exposed to infectious diseases; the dangers in the two cases are of the same order of probability. P. L.-B.

Radiodiagnosis

Dennis, C. E. Pulmonary fibrosis after gassing, as shown by X-rays. *Med. J. Austral.*, 1919, Nov., 372.

In the radioscopic examination of subjects gassed more or less severely by chlorine, phosgene, or hyperite, who have for some time suffered from cough, wasting, anorexia, nausea, retrosternal pains, accompanied by a diminution of the vesicular breath sounds and a slight dullness on percussion without there being tubercle bacilli in the sputum, the author has proved that the apices cleared up uniformly, but that the clearness of the thorax as a whole was diminished from the fact, so it seemed, of the thickening of the peribronchial tissues radiating from the hilus of the lung; further, the shadow of the hilus was increased and presented speckling due to hypertrophy of the glands; the movement of the diaphragm in deep inspiration was much reduced or almost absent, but persisted in coughing, an indication of the functional nature of this limitation of movements which is probably due to the inconvenience created by a full respiration and accounts for the diminution of the percussion note and the vesicular breath sounds. The radiograph confirmed the statement that the cause of the diminished clearness of the pulmonary field was chiefly due to proliferation of the fibrous tissue of the lung, more marked usually on the right side.

Later, the author had the opportunity of examining some cases in which the gassing took place at an earlier date. Radioscopy gave the same picture, but the limitation of the movements of the diaphragm were, on the whole, less. In the plates were seen linear shadows, more or less large with fairly clear outlines, radiating from the hilus to the periphery of the lungs, shadows of the glands and often small round or oval spots scattered between the periphery and the hilus which probably represented the shadow of the crossing of the bronchioles surrounded with fibrous tissue. When there was much bronchial secretion, a mottled appearance was seen, but always less localized than in tuberculosis. These modifications are not always proportional to the severity of the original intoxication.

The peribronchial sclerosis, which is not met with in ordinary bronchitis, is found in subjects who have lived for a long time in a dust laden atmosphere, particularly in the case of miners. P. L.-B.

Duval. Colectomie totale dans le traitement des cancers coliques. [**Total colectomy in the treatment of cancer of the colon.**] *Bull. et mém. Soc. de chir.*, 1919, Oct., 1365. (*J. de radiol. et d'électrol.*, 1920, **4**, 136.)

Post-operative radiological examination shows that at the level of the anastomosis, the passage of intestinal contents is very easy; the last coil of small intestine presents neither dilatation nor abnormal peristaltic or antiperistaltic movements. S. U. L.-B.

Groedel. Typhusdiagnose aus dem Röntgenbild. [**Diagnosis of typhoid fever by means of the X-ray plate.**] *Frankfurter Röntgengesellschaft,* 1921, Jan. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 83.)

The author showed an X-ray plate of the shoulder and upper arm of a patient aged 45. The physician in charge of the case stated that septic fever had existed for about four weeks, which could be referred to an abscess of the axillary glands. Incision of the abscess did not lower the fever, and disease of bone was suspected. On the X-ray plate there was found a small longish clear zone beneath the cortical layer, owing to which the latter had bulged forward to a small extent. Periosteal separation was not present. Without knowing the history of the case the author recognized that the plate was characteristic of typical typhoid bone disease. The opinion was communicated to the physicians who subsequently found a distinctly enlarged spleen, several rose spots, and a strongly positive Widal reaction. A few days later defervescence occurred, the symptoms disappeared, and, 14 days after the first plate was taken, a new plate showed normal conditions. In the meanwhile the bones, and especially the long bones, were examined for further evidence of bone lesion, but with negative results.

The X-ray appearance of typhoid lesions of bone is little known: the author showed four analogous cases observed during the war. Recognition of the value of the X-ray plate in this variety of bone disease, is not unimportant, since disappearance of symptoms is not always so rapid as in the case described. Sometimes the bone-condition persists for years. Inasmuch as typhoid bacilli are invariably found in typhoid nodes, they may be occasionally the seat of infection in typhoid carriers. At all events, they are so characteristic of the X-ray plate, that they may assist a diagnosis which is often difficult in regions free from the disease.

S. U. L.-B.

Sgalitzer, M. Über den röntgenologischen Nachweis nicht schattengebender Fremdkörper in Empyemhöhlen. [**On the presence of opaque foreign bodies in empyema cavities revealed under Röntgenology.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 332.

Sgalitzer gives the results achieved by the discovery through Röntgen ray exposure of foreign bodies left in empyema cavities.

He writes: 'that foreign bodies which have not been visible under X-rays or reproduced under Röntgenography are too often the cause of empyemic suppuration is not sufficiently taken into account, and yet it is well known that under a protracted operation of the empyemic cavity, a torn, or a whole drainage tube or piece of gauze tampon has inadvertently been left in the cavity, thus being the immediate cause of suppuration and consequent failure to heal.'

The question now arises if Röntgenology is limited to the localization of metallic or other such dense foreign bodies in empyemic cavities, or whether it will be possible to make other less dense matter visible by this means? Before answering this question Dr. Sgalitzer enters upon a short disquisition on the density and Röntgen demonstrativeness of rubber tubing, which most frequently is left in the cavity. For localizing such bodies the writer gives the method of procedure: 'Fistulous tracts are filled with contrast mixture of bismuth vaseline, and zirkon oxide, and so become easily reproduced on the Röntgen plate, thereby revealing the cause of suppuration. There follows careful observation of the cavity on the Röntgen screen, exact localization of the foreign body, and its extraction by means of dressing forceps. Use of the cystoscope or similar instrument is seldom necessary, the more so as the pus creates a non-transparent medium on this instrument. When, however, its use is necessary, a small Farabœuf grasping forceps must be used for the extraction of the foreign body, an operation which should be performed with the greatest care, and certainty in knowledge of the use of the instrument.

Giving several cases in which successful extractions were made and the patients restored to complete health, Dr. Sgalitzer sums up his article as follows: 'as touching foreign bodies in empyemic cavities which have escaped observation under Röntgen rays, these can be made visible to Röntgen tests by means of contrast-filling of the said cavities. Their recognition is made possible inasmuch as the contrast mixture is caught and retained in the fibrous threads with which the forgotten tube has become filled, while in the case of gauze tampons these become impregnated with the injection and in like manner are revealed by their increased density. The extraction of these bodies, which have only become visible by this method, results under Röntgen control in their removal through the sinus by means of forceps.'

A systematic examination of all patients suffering from pleural empyema of long standing, would certainly reveal that which the ordinary Röntgen ray examination has failed to bring to light. F. E. R.

Radiodiagnosis

Goetze, O. Ein neues Verfahren der Gasfüllung für das Pneumoperitoneum. [**A new method of producing pneumo-peritoneum.**] *München. med. Wchnschr.*, 1921, **68**, 233. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 95.)

The author now places the patient in a lateral position with the pelvis greatly raised when about to induce pneumoperitoneum. In this position the pressure within the pelvis is below that of the atmosphere, so that when the abdominal wall is punctured 3–4 fingers' breadth on the umbilical side of the anterior superior spine of the ilium, gas is sucked in. When this occurs the surgeon has evidence that the abdominal cavity has been entered. By this procedure damage to the intestine can be avoided with certainty.
S. U. L.-B.

Jaensch, W. [B.] Über das Röntgenbild der Pneumonokoniosen, insbesondere ihre grobknotige Form. [**On the Röntgen picture of pneumokoniosis, especially in its densest form.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 299.

The object of the writer of this article is to show the differentiation between pneumokoniosis and ordinary tuberculosis, for the clinical symptoms in both forms of disease resemble each other closely. One point of distinction he gives is that in pneumokoniosis it is seldom that the apex of the lung is affected, the disease mostly affecting the underlying parts of the upper lobe of the lung. It is, according to the Röntgen picture, more evenly distributed over both halves of the lungs than in advanced tuberculosis. Also dyspnoea may be very marked in pneumokoniosis, whereas even in very advanced tuberculosis it is mostly absent. The tuberculin reaction is negative.

According to the Röntgen photographic demonstrations, the shadow pictures differentiate between miliary tuberculosis and pneumokoniosis by the variation in the size of the shadow groups, leaving the apex almost free. Anthracosis and chalicosis reveal wider and more irregular patches.

In a series of photographs the author shows the varied forms of lung patches caused by the different types of lung troubles, namely, syphilitic pneumonia, pneumokoniosis, &c., and lung affections caused by iron dust inhalations. F. E. R.

Vogt, E. Zur Röntgendiagnostik des Magen-Darmkanals des Neugeborenen. [**Röntgen diagnosis of the stomach of newly-born infants.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 287.

Vogt has chosen for the subject of a short comprehensive article, the different effects of feeding with a mixture of citobarium and mother's milk or cow's milk, on the intestinal canal of new-born babies, as compared with the use of undiluted milk, and has shown in detail the effect on the intestinal canal by a series of sketches from X-ray photographs.

For a contrast meal, which after a series of experiments the author has found entirely satisfactory, 20 to 30 gm. of citobarium in a thin suspension sufficed; the citobarium doses were varied between 20 and 40 gm. according to the age and size of the child. The best method of mixing was with water—oil, milk, or paraffin having proved much less satisfactory.

The infant's stomach, says Dr. Vogt, after it first begins to absorb nourishment is more of a fish-hook than of syphon form. The empty stomach is cylindrical, the body axis and the stomach axis forming a sharp angle. He cannot make any definite statements in regard to the duodeno-jejunal flexure, the jejunum never being equally filled and its contents being unequally distributed.

The writer sums up his observations by stating that a meal of citobarium and mother's milk takes from 1½ to 3 hours to pass through the stomach, somewhat longer if mixed with cow's milk, and an unmixed meal of mother's milk takes from 4 to 5 hours to digest completely. He reckons as an outcome of his clinical observations, that in new-born infants 5 to 6 meals *per diem* of the contrast mixture results in 3 to 4 intestinal evacuations *per diem.* F. E. R.

Radiotherapy

Jess, F. Über Speicherung von Jod im Karzinomgewebe. [**On the storing of iodine in carcinomatous tissue.**] *München. med. Wchnschr.*, 1921, **68**, 323. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 96.)

The object of the communication is to demonstrate and evaluate secondary radiations after introduction into the body of substances giving rise to specific secondary radiation.

In order to determine the quantity of iodine contained in them, the author examined severally the organs of a patient who had died of carcinoma of the gall-bladder. For four weeks preceding death the patient received iodine internally and subcutaneously. The following quantities in milligrams of iodide of potassium were found in 100 gm. of organ substance:

Thyroid gland, 50·6.	Liver, 14·6.
Digestive tract, 28·2.	Spleen, 13·9.
Skin, 23·9.	Uterus, 12·3.
Lungs, 23·3.	Kidneys, 11·5.
Blood, 21·0.	Heart-muscle, 8·6.
Tumour, 21·0.	Skeletal-muscle, 7·2.
Ovary, 17·0.	

He raises the question whether it will be possible to utilize the property of tumour-tissue to store within its cells a body which produces a characteristic secondary radiation, and thinks so new a departure in X-ray therapy of malignant neoplasms must be left to future research. S. U. L.-B.

Czepa, A. Erstickungstod nach Röntgenbestrahlung eines Mediastinaltumors (Lymphogranuloms). Ein Wort zugunsten der Probebestrahlung. [B.] [**Death by suffocation after radiation of a mediastinal tumour (Lymphadenoma). A word in favour of a trial exposure to radiation.**] *Strahlentherapie*, 1921, **12**, 239.

While so much has been written about lesions of the skin following upon radiation the references in the literature to damage to other structures are by comparison so meagre, and it so seldom happens that death is either directly or indirectly due to radiation that this case is recorded at some length, as being of special interest. Hitherto the deaths that have been recorded have mostly resulted from serious alterations brought about in the blood picture in cases of acute leucaemia or from intestinal necrosis after intense radiation in gynecological cases.

Details of the case are set out in full, with the family and personal history of the patient (a woman), progress, treatment, and post-mortem findings. A reproduction of a radiograph of the chest is also given. The X-ray treatment consisted of radiation through two ports of entry. Each 10 cm. × 15 cm.—one dorsal and one in front. The same dose was administered to each in a single sitting, the data being as follows: 35 cm. spark gap, Bauer 10, 3·0 mm. aluminium filter, gas break, 1,250 interruptions, 2·0–2·5 m.a., target-skin distance 24 cm., time 15 minutes. This was estimated to give 8 H. or 75 per cent. of the erythema dose. About $2\frac{1}{2}$ hours after the conclusion of the sitting the patient became markedly dyspnoeic and cyanosed, and finally died two hours after the onset of symptoms. Post-mortem examination showed that death was due to obstruction of the trachea by an oedematous mass of lymphadenomatous glands. The innominate artery and superior vena cava were also involved. Detailed description of both macroscopic and microscopic appearances are given.

The author estimates that the dose actually reaching the tumour was about 20 per cent. of the erythema dose, which is small as compared with the 60 per cent. for sarcomata and the 50 per cent. dose in tuberculous adenitis advocated by Seitz and Wintz, but which, nevertheless, proved in this particular case to be too large. It is interesting to note in the literature the dosage prescribed by various authors for mediastinal tumours. Unfortunately, only a small proportion of papers are of real value in this respect, for many give only approximate working directions and others give no practical data as to radiation at all. Furthermore, on looking through the literature of the subject, it becomes apparent that from the descriptions of the cases there given a definite conclusion as to the real nature of the tumours can practically never be reached. The terms pseudo-leucaemia, lymphosarcoma, and lymphadenoma are used almost synonymously, and cases where the diagnosis of lymphadenoma is based upon histological evidence are very few.

The author concludes by urging that all cases of mediastinal tumour, goitre, or hypertrophic thymus, when danger to life would occur from compression of the trachea if there were swelling of the irradiated tissue, should be submitted as a precautionary measure to a small trial dose before heavier dosage is undertaken, or, better still, should be treated only by small doses frequently repeated.

A comprehensive bibliography is appended. E. M. W.

Klewitz, F. Über Röntgentiefentherapie bei inneren Krankheiten. [**Deep X-ray therapy in internal disease.**] *Strahlentherapie*, 1921, **12**, 203.

A general review of radiotherapy of internal disease shows a quite noticeable progress. Of the mode of action of the rays in individual diseases admittedly little is yet known. It has still to be determined whether further progress depends upon improvements in technique or upon some means of sensitizing the diseased part to the rays, or upon making use of the secondary radiation produced in the tissues.

This paper gives an account of the author's personal experience in the treatment of disease. The question of dosage is important. He has abandoned both the Kienböck radiometer and the Fürstenau intensimeter as being too inexact in estimating the dose. For the last 18 months he has used the 'biological unit' of dose—i. e. the maximum amount which the skin will tolerate without reaction. This dose is obtained with 2·0 m.a., high tension voltmeter reading of 156–160, 0·5 mm. zinc filter, 23·0 cm. target-skin distance in 55–60 minutes, or with 3·0 mm. aluminium filter in 35–40 minutes. The proportion of the incident dose which reaches various depths in the tissues is estimated by means of a phantom and a Kienböck radiometer. The deep dose obtained is sufficient to deal with any condition except carcinoma.

The diseases dealt with are:—

(1) Diseases of the blood: myeloid leucaemia, lymphatic leucaemia, polycythaemia, haemophilia.

(2) Tuberculosis: pulmonary tuberculosis and tuberculous pleurisy, laryngeal tuberculosis, tuberculous adenitis, tuberculous peritonitis.

(3) Non-tuberculous diseases of the respiratory system: bronchial asthma, emphysema with chronic bronchitic and asthmatic symptoms.

(4) Tumours: mediastinal, including tuberculous swellings, sarcomata, lymphadenoma; hypertrophic prostate.

(5) Exophthalmic goitre.

(6) Neuralgia: trigeminal neuralgia, plexus neuralgias, sciatica.

(7) Chronic rheumatoid arthritis.

In each case an outline of the treatment adopted is given.

Emphasis is laid upon the necessity of proceeding with caution in the treatment of diseases of the blood, when the changing blood count must be carefully watched. A rapid destruction of leucocytes in the leucaemias must be carefully avoided. Haemophilia is treated by radiation of the spleen with small doses. A case of severe haemorrhage into the bladder stopped bleeding almost immediately after a single small dose to the spleen.

Caution must also be used in treating tuberculosis: overdosage may result in rapid aggravation of the disease. Only advanced cases of pulmonary tuberculosis were treated, and the numbers are too small to enable a useful opinion upon the treatment to be formed. The results of treatment of tuberculous adenitis are good. In the author's view suppurating or caseous glands require surgical treatment.

Non-tuberculous conditions of the respiratory tract respond well, but whether the results will be permanent or not remains to be seen.

In exophthalmic goitre careful selection of cases is necessary. In certain patients a temporary lowering of the sugar content of the blood has been noted. Following this observation a few diabetic cases were submitted to radiation of the thyroid, but the results do not permit of the drawing of definite conclusions. One case, however, remained unaffected and another showed some increase in the sugar content.

In neuralgia and rheumatoid arthritis the results are very variable and on the whole not encouraging. E. M. W.

Béclère. Que doit-on espérer et que peut-on craindre de l'emploi, en radiothérapie profonde, de rayons très pénétrants? [B.] [**What should be hoped and what feared from the use of very penetrating rays in deep radiotherapy?**] *J. de radiol. et d'électrol.*, 1921, **5**, 385.

The author points out that the use of very penetrating X-rays entails a slower decrease in the doses successively absorbed: this gives to the radiotherapist two possibilities which must be clearly distinguished. The first is the possibility of obtaining a much more equally distributed dose throughout the lesion than formerly when treating a subcutaneous lesion; the second is the possibility of giving greater doses beneath the skin without damage to that structure. He says that the former is an undoubted advantage, but not so the second, since in some cases it becomes dangerous or even fatal. The question of radiotherapy in tuberculous lesions is then considered. Stephan, of Frankfurt, has the impression that in spite of the progress in apparatus and technique the therapeutic results are less good, to which the author states there can only be two interpretations if the view is correct; either the very penetrating rays now used have a less favourable action than the less penetrating rays formerly used, or the actual dose given is excessive. The first is stated to be contradictory to the results of the researches of Krönig and Friedrich on the biological action of penetrating rays of different wave-lengths when using tadpoles. A short account of Stephan's clinical results is given, and the author then states that in the radiotherapy of tuberculous affections the use of the most penetrating rays is not always the best, but that often smaller doses are much preferable.

The radiotherapy of leucaemia. The author states that lymphatic and myeloid leucaemia are nearly related to cancer from the general pathological point of view, and that X-ray therapy is the only treatment that can be recommended. Rosenthal's method at Budapest is shortly described, by which the spleen in myeloid leucaemia is made to absorb at a single séance the maximal dose of 1,050 to 2,000 units measured by Fürstenau's intensimeter. Rosenthal approves of the method, but Béclère points out that almost immediately after irradiation severe reactions are seen. These are described as they occurred in three out of eleven cases that ended in death, and Béclère states that it cannot be doubted that they are due to the radiations.

Intestinal lesions. Various lesions of the mucosa of the intestine have been seen after irradiation of lesions such as myomata or uterine carcinoma; these chiefly affect the rectum or pelvic colon. Usually the symptoms disappear and the lesions heal after a short time.

Changes in the blood. These are more to be dreaded than the preceding lesions because the microscope alone reveals them. The author refers to the work of Seitz and Wintz in treating uterine cancer with X-rays and mentions that the red cells as well as the white are affected. It is approximately six weeks after deep irradiation before the blood has completely recovered, sometimes even eight weeks. For this reason a second dose should not be given for six weeks. In all cases, if the blood lesions persist, treatment fails.

Specific doses. Reference is made to the work done at the Freiburg (Breisgau) and Erlangen schools and the radiotherapist is warned against the tempting but too theoretical simplicity of the ideas of researches otherwise remarkable. The most important point to inquire into is whether the correctness and severity of the doses have been proved desirable from the clinical point of view. The specific 'doses' formulated by Seitz and Wintz are criticized in the following way.

Castration dose. The author has come to the conclusion, with most of his colleagues, that this varies in the individual case, since the radiosensibility of the ovaries varies with the age of the patient.

Sarcoma dose. As regards the treatment of sarcoma therapeutic progress is stated to be much less than that of the technique, as shown by the comparisons made by Jungling, which are referred to at some length. The conclusion is that the radiosensibility of sarcomata between the lymphosarcomata on the one hand and the osteosarcomata on the other varies very greatly.

Carcinoma dose. Epithelial cells are not so variable as regards radiosensibility as are sarcoma cells, yet Kehrer finds that in treating carcinoma of the neck of the uterus the lethal dose varies between wide limits. Kehrer's technique is described shortly.

In conclusion, the author says that the radiotherapy of sarcomata and carcinomata cannot be placed within such simple and narrow formulae as those of Seitz and Wintz. Penetrating rays are not always necessary, nor without danger, nor efficacious. P. L.-B.

Radiobiology

De Niord, R. N., Schreiner, B. F., and **de Niord, H. H. The effect of Röntgen rays on the metabolism of cancer patients.** *Arch. Int. Med.*, 1920, **25**, 32. (*J. de radiol. et d'électrol.*, 1921, **5**, 284.)

The authors have studied the chemistry of the blood of 40 cancer patients who had undergone radiotherapy, using as controls healthy subjects irradiated in the same manner and non-irradiated cancer patients. Their conclusions are as follows: The blood urea and creatinin do not show any modification characteristic of cancer. The slight increase in the uric acid which is produced transiently after exposure to the rays is only the result of the destruction of the nuclei, and in no way a characteristic indication of malignancy. The chloride content of the serum in cancer patients is not influenced either by the presence of the tumour or of the irradiation. The cholesterine, the fatty acids, and the total fat are usually increased in malignant cases. The irradiation determines the rate of increase of the cholesterine, but this increase has no bearing on the type of tumour and is probably related to the autolysis of cells produced by the X-rays. The amount of fatty acids is almost always above normal in the blood of cancer patients. After irradiation it diminishes markedly in half an hour after exposure, and still more so after 24 hours, but the cause of this diminution is not known as yet. The blood-sugar and the activity of the amylase are not characteristic in cancer patients. The action of the rays on the sugar content is the most variable; however, the patients who have received the largest doses show for a time a marked decrease in the sugar; irradiation increases oxidation of the blood-sugar, but the same phenomenon is seen in normal cases.

Lastly the authors have measured the relation of the volume of the plasma to that of the cells of the blood: it is not altered by irradiation and is of no diagnostic value in cancer. P. L.-B.

Russ, S., Chambers, H., and **Scott, G. M. On the local and generalized action of radium and X-rays upon tumour growth.** *Proc. Roy. Soc.*, 1921, B. **92**, 125.

The subject of the successful treatment by radiation of a tumour in the animal body is one which resolves itself, broadly speaking, into the action of the radiations on (1) the tumour-cells and on (2) the animal itself. A *résumé* of the effects observed by the authors and others leads to three main issues on which the considerable experimental work of the paper is based viz.:

The effects of the rays in various doses upon

(*a*) Malignant cells before inoculation.

(*b*) Normal animals—(1) Body growth. (2) Subsequent inoculation of malignant cells.

(*c*) Normal animals which are bearing tumours.

The investigation was carried out upon rats with three distinct types of tumour, viz.: Jensen's rat sarcoma, with which the majority of the experiments were made, a very slowly growing rat sarcoma, and a rat carcinoma.

(*a*) Following the method of Wedd and Russ, several slices of excised tumour, having been exposed aseptically to β-rays from 20 mgm. of $RaBr_2\,2\,H_2O$ for various times, were implanted into normal rats. The subsequent tumour growth was accurately recorded and compared with controls. It was found that the lethal dose, viz. 35 minutes, for Jensen's rat sarcoma and the rat carcinoma employed, was rather lower than that required for the slowly growing rat sarcoma. Further, as the dose decreases from the lethal a reduced rate of growth changes into a rate slightly quicker than that of the untreated tumour, being 1·35 times the normal when the initial tumour material received 12 seconds' exposure.

(*b*) The effect of various doses upon the body-weight of normal rats was determined by placing the animals 20 cm. below the anticathode of a Coolidge tube, the radiation being standardized, as far as possible, by means of a gold-leaf electroscope. Batches of animals received daily doses of X-rays, lasting from 2 seconds to 1 minute and maintained from 4 to 9 weeks. The 1-minute exposures were deterrent to increase of body-weight, but under an exposure of 12 seconds the weight increases 15 per cent. more rapidly than that of untreated animals of the same initial weight.

Experiments were made to determine whether the immunity to tumour growth, imparted to rats exposed to small daily doses of X-rays prior to inoculation, could be rendered complete by varying the period over which the daily 12-second dose was continued. Absolute immunity has not been found possible. However, with 77 rats so treated there was, on the average a reduction in tumour growth of 40 per cent. as compared with that in 77 unexposed animals.

(*c*) The authors have drawn distinctions between three varieties of exposure viz.: (1) Exposures in which the animal does not share to an appreciable extent in the radiation which the tumour receives—localized exposure to β-rays; (2) vice versa—tumour screened from the rays; and (3) a generalized exposure of the whole body to X-rays.

(1) A series of experiments similar to that of section (*a*), except that the tumour was treated while growing in the animal, gave results strikingly similar. The minimum time required to prevent tumour growth was appreciably the same, and again the effect of small radiation doses was to increase rather than to diminish growth. With batches of animals receiving weekly doses of from 10 minutes to 12 seconds it was shown that, 'while a weekly exposure of 10 or 5 minutes checks tumour growth, a reduction to 1 minute has an opposite tendency.'

(2) Animals inoculated with the sarcoma in the middle of the back

were submitted to daily 12-second doses of X-rays, the graft being screened by 2 mm. lead. The treatment lasted one month, and results from 24 animals showed a decreased susceptibility to tumour growth in the 12 rats receiving generalized radiation.

It was apparent that the effects observed in (1) and (2) acted in opposite directions. In order to determine which outweighed the other, when tumour-bearing animals received generalized irradiation at frequent intervals, two batches of rats were compared, the one receiving daily radiation doses of from 5 minutes to 2 seconds, the other none. Daily exposures of over 1 minute result in reduced rate of tumour growth, but the body-weight suffers. With smaller exposures there is less effect in slowing up the tumour, but the body-weight is accelerated over the normal. There appears to be less restraint on the tumour when it is allowed to share in the dosage given to the body.

The bearing of the results upon the radiological treatment of malignant disease in man appears to be two-fold. Firstly, as the uniform irradiation of a large tumour is hardly possible, the authors point out that, should the quantity of radiation reaching the confines of the growth be only a few per cent. of the lethal, there might be a stimulative rather than an inhibitive action upon the malignant cells at these parts. Secondly, although ample evidence shows that large generalized doses of radiation lower the normal resistance to tumour growth the converse holds for very small doses given frequently. The authors conclude that it is therefore a rational measure to supplement local intensive irradiation of a tumour by a feeble generalized irradiation of the patient, care being taken wherever possible not to expose the tumour-cells to this radiation. L. H. C.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

TUBERCULOSIS

Epidemiology. Bushnell devotes special attention to the rôle of Pirquet's test, which he believes is destined to become of increasing importance in the epidemiology of tuberculosis. Applied wholesale in conjunction with vaccination for small-pox, Pirquet's test could be made the foundation for a systematic tuberculosis census yielding important information as to the types, morbidity, and mortality of this disease. The later history of the children giving a positive reaction could then be compared with that of the negative cases, and information obtained as to the relative probability of the future development of manifest tuberculosis in the two classes. It is further urged that children, giving a negative reaction, should be tested again every year or oftener until a positive reaction is obtained. Such a census would not only yield information of value to posterity, but it would, in the individual case, be a step towards keeping the child under specially hygienic conditions during the period immediately after the first infection. There can be no doubt that the first half-year after infection is a critical time for the child, and that its adequate supervision at this time would do more to lower the morbidity and mortality from tuberculosis than anything except preventing the infant from coming into contact with the consumptive.

Against Bushnell's proposal of a tuberculosis census pivoting on Pirquet's test, a criticism of the value of this test by Hamburger of Graz may be quoted. He calculates that the margin of error may be as great as 40 per cent., and that the chief fault of Pirquet's test is that it underestimates the frequency of infection. He refers to two series of investigations carried out in Vienna, the one with Pirquet's cutaneous inoculation, the other with local subcutaneous inoculation. The first showed positive results in 56 per cent. of children between the ages 11 and 14, while the second showed positive results in 95 per cent. Hamburger recommends the following routine. Every child is first tested by the cutaneous or percutaneous reaction with concentrated tuberculin. Those who do not give a positive reaction are then given, 24 or 48 hours later, a subcutaneous injection of 0·01 mgm. of tuberculin. The cases which are still negative after this test are given, 24 hours later, a second injection of 0·1 mgm., and if this provokes no reaction, 1 mgm. is injected subcutaneously after 24 and within 48 hours of the previous injection. Only in doubtful cases is it necessary to give a final injection of 10 mgm. to prove the child's freedom from infection.

Hamburger admits that this system is laborious and tedious, whereas Pirquet's test is alluringly simple. But it is 'absolutely unreliable', and as the margin of error varies within wide limits, there is no possibility of correcting Pirquet's findings so as to show the actual incidence of infection. The result of Pirquet's test depends largely on such factors as: (1) the character of the instrument used and of the depth of the abrasion; (2) the length of time during which the tuberculin acts; (3) the potency of different series of tuberculin supplied by the same maker; (4) the number of times the test has been carried out, more positive results being obtained with multiple tests than with a single test; and (5) the time of year at which the test is made. Hamburger's indictment of Pirquet's test applies only to the negative reaction: a positive reaction is reliable, and in the case of a wholesale tuberculosis census, the cutaneous or percutaneous test could first be made, and only the persons failing to react need submit to the further test elaborated by Hamburger.

Armstrong has extracted some curious findings from a Pirquet survey of children in Framingham,—a representative American community of about 16,000 people living under typical American industrial and social conditions. He found that the incidence of both infection and disease varied greatly with race stock. A positive Pirquet reaction was obtained in 33 per cent. of all the children between 1 and 7, but while of the Irish and Irish-American children of this age only 30 per cent. gave a positive reaction, as many as 51 per cent. of the Italian children did so. On the other hand, nearly ten times as much active tuberculosis was found at all ages among the Irish as among the Italians.

Kretschmer performed Pirquet's test on 180 Berlin children up to 14 years of age in whom tuberculosis was suspected on account of the history or clinical symptoms, and obtained a positive reaction in 42·2 per cent. as compared with a percentage of 49 found by Synwoldt at Rostock and one of 65 by Klose at Greifswald. On the other hand, the percentage of those giving a positive reaction with bovine tuberculin was much higher among the Rostock children (35 per cent.) than among those at Greifswald (5·34 per cent.) or at Berlin (7·8 per cent.). The low percentage of positive reactions among the Berlin children is attributed by Kretschmer to the lowered immunity caused by the under-nutrition prevalent in the large towns of Germany, while the high percentage of positive reactions with bovine tuberculosis at Rostock as compared with Berlin is probably due to a better veterinary supervision of the Berlin milk and consequently less opportunity for infection with bovine tuberculosis.

Calmette states that in 1908 Cummins drew attention to the absence of tuberculosis, apart from a few imported cases, among the natives of the Soudan province of Bahr-el-Ghazal. Ziemann had never seen a case in the Cameroon hinterland, whereas the disease is frequent in Natal among the Zulus, in the Transvaal, and in Madagascar, and its intensity is almost as great as in Europe in all the towns of North Africa. On the other hand, it is rare among the nomad tribes of the Arabs and Berbers who live at the south of the Atlas chain. In East Africa Peiper observed that tuberculosis, which was rare among the negroes in the villages, was common in agglomerations consisting of Indians, Arabs, and Europeans. Throughout East and Equatorial Africa there are only a few nomad tribes on the confines of the Sahara and Nubian desert who are practically free from the disease. In the most civilized countries tuberculosis is responsible on an average for 12 per cent. of the deaths, sometimes for 19 per cent., as in Norway and Sweden, and never less than 7·4 per cent. in the most privileged countries, such as Belgium, Italy, Portugal, and Spain. High as these figures are, they do not correspond to the facts, because many tuberculous subjects succumb to other affections which tuberculosis has aggravated.

The great increase in the prevalence of tuberculosis in Germany and Austria during the war, to which attention has been previously drawn (vide *Medical Science*, 1920, **2**, 225; 1921, **3**, 486), is discussed by numerous German writers such as Hamel, Ickert, Kirchner, Möllers, Peller, Reiche, and Umber, the causes assigned being under-nourishment, lack of coal, defective housing accommodation, scarcity of soap and disinfectants, insufficient clothing, mental and physical strain, and the influenza epidemic of 1918. Hamel states that the tuberculosis mortality in Germany, which had been more than 30 per 10,000 in 1884, had fallen in 1913 to 14 per 10,000. In other words, in the last years before the war there were 100,000 fewer deaths from tuberculosis than 30 years previously. A distinct rise in the tuberculosis mortality occurred in 1914 and 1915, the death-rate was more than doubled in 1916, and there was a still greater rise in 1917, which was maintained in 1918 when there were 40,000 more deaths from tuberculosis in Germany than in 1913. In the latter part of 1918 a decline in the mortality took place, so that in 1919 the death-rate was about the same as in 1917 or about 65 per cent. more than in peace time. Möllers of Berlin and Selter of Königsberg also testify to the decline in the tuberculosis mortality since 1919 owing to the improvement in the supply of food.

According to Kirchner, before the war the tuberculosis mortality was lowest in Saxony and highest in Prussia, Hamburg, Wurtemberg, Hesse, Bavaria, and Baden in the order named. During the war the increase differed accordingly. In neutral countries it was lowest in Denmark, higher in Holland, and higher still in Switzerland. In Sweden and Norway the mortality from tuberculosis, which has always been high in these countries, did not show any further increase during the war. The age period at which the greatest increase in mortality occurred during the war was from 15 to 20. As regards sex distribution, whereas during peace time the tuberculosis mortality was higher in the male than in the female sex except for the age periods 5–20 and 25–40, during the war the increase was higher in the female sex at all age periods except from 10–15 and from 25–30. Kirchner points out that the death-rate rose later in the country, was always at a lower level, and began to sink earlier than in the towns. According to Hamel the number of deaths from tuberculosis in the country districts of Prussia rose from 25,208 in 1913 to 36,207 in 1917, or more than 40 per cent.

Reiche gives statistics showing that the mortality from pulmonary tuberculosis in the town of Hamburg progressively diminished from 1890 until the beginning of the war, and suddenly increased from 1915 until 1918 when it fell again. Thus the mortality from pulmonary tuberculosis, which was 26·2 per 10,000 in 1890, fell to 11·2 in 1913, was 12·9 in 1915, 14·4 in 1916, 20·7 in 1917, 22·6 in 1918, 17·3 in 1919, and 14·6 in the first half of 1920. These statistics are confirmed by Reiche's experience in hospitals, where he was struck by the prevalence of acute forms, the frequency of recent attacks in old persons, and the large number of children with glandular and osseous tuberculosis.

Umber has compiled statistics of 2,416 Charlottenburg children aged from one month to 14 years showing the incidence of tuberculous infection as determined by the Pirquet reaction, the frequency of clinical tuberculosis, and the mortality from tuberculosis in the two years preceding the war, the period 1914–18, and 1919–20. In the pre-war period no child was infected during the first three months of life, whereas during and after the war the number of infections ranged from 2·4 to 4·7 per cent. After the second year the number of children infected considerably and progressively increased compared with the pre-war period. It was noteworthy that a relatively large number of children (52 per cent.) aged 3–4 were infected in 1916–18, as well as of children aged 5–6 in 1919 (57·5 per cent.), whereas between the ages of 11 and 14 the number of those infected during and after the war (60–66 per cent.) was not much higher than in 1912–14 (56 per cent.). A relatively high proportion (70 per cent.) of children infected in the fifth and sixth years of life showed clinical evidence of tuberculosis in 1920, whereas older children showed a much lower incidence (39–15·4 per cent.). The mortality among children in the second to tenth years of life was much higher than in those aged from 11 to 14 who had been well nourished during their early years.

Ickert states that the mortality from tuberculosis among children and young persons rose during the war both in Germany and Holland, but was about ten times as high in Germany as in Holland. The various age periods were not equally affected, the increase in mortality in Germany among young children being considerably over 100 per cent., among school children about 50 per cent., and in persons aged from 15 to 20 up to 200 per cent.

Peller states that in Vienna the tuberculosis mortality before the war was higher among men in every district than among women. In 1919, on the other hand, in a considerable number of districts it was lower among men than among women, and in only three districts was it higher among men. The districts which showed a great increase in tuberculosis mortality were those which before the war had been inhabited by a well-to-do population. In the poorer districts, though there was a greater number of cases of tuberculosis than before, there was not such a relatively large increase, possibly owing to the fact that during the war a considerable proportion of those affected in the poorer districts succumbed.

Carbonell presents statistics showing that there is an increase in the tuberculosis mortality in the Argentine Republic in spite of a decrease in the general mortality. Hygienic and prophylactic measures have lowered the general mortality and the death-rate from infectious diseases other than tuberculosis, which does not appear to have been affected thereby.

Aetiology. Pearl has made a thorough study of the family histories of individuals afflicted with tuberculosis, and of others free from tuberculosis, the two groups being taken from the same economic and social strata. Although his report is only preliminary, and his investigations are still proceeding, Pearl claims that he knows of no data for the study of the aetiology of this or any other disease which begin to approach his own in respect of comprehensiveness, detail, or accuracy. In one of his tables he publishes the family histories of 38 tuberculous and 19 non-tuberculous persons selected at random from the working-class population of Baltimore. More than 5,000 blood relatives of these 57 persons were included in this investigation, which extended over five generations. When all these generations were taken together, it was found that 7 per cent. of the blood relatives of the original tuberculous persons were themselves tuberculous, whereas only 1·2 per cent. of the blood relatives of the original non-tuberculous persons were tuberculous. In other words, it would appear that a tuberculous person chosen at random from the working classes has nearly six times as many tuberculous blood relatives as a non-tuberculous person taken from the same class. The same kind of difference appeared in each generation. Where there was no immediate tuberculous ancestry (parents and grandparents non-tuberculous) 7·4 per cent. of the offspring proved to be actively tuberculous. This proportion was probably a little less than the normal rate of tuberculosis among the working classes in Baltimore. Of this 7·4 per cent., nearly a fourth (22·2 per cent.) had lived for some time in close contact with cases of active tuberculosis. On the other hand, of the 92·6 per cent. of non-tuberculous offspring of non-tuberculous ancestry, only about one-tenth (11·2 per cent.) had been in close contact with an active case. Thus, twice as many of the tuberculous offspring of non-tuberculous ancestry had been in close contact with active tuberculosis as was the case with the non-tuberculous offspring of non-tuberculous ancestry. It was also found that as the amount of tuberculosis in the direct ancestry increased, the amount of tuberculosis in the offspring increased also, but the disturbing factor was noted that the rate of close contact with open active cases increased far more rapidly than did the rate of incidence. Where one or both parents were actively tuberculous, practically all the offspring who developed tuberculosis had been in close contact with another active case, usually, of course, the parent or parents. To the argument that these findings pointed as much to infection as to hereditary predisposition, Pearl replies that where one or both of the parents were actively tuberculous, virtually three-fourths of their non-tuberculous offspring had been in just as close contact with active open cases as their brothers and sisters who developed the disease. Pearl admits that the numbers with which he has dealt must be multiplied many fold before definite conclusions can be drawn as to the comparative importance of heredity and infection. His figures indicate that familial contact with active open cases is, beyond question, a factor in determining the incidence rate of clinically active tuberculosis. ‘It appears equally obvious, however, that it certainly does not account for the whole, and probably accounts only for a small part, of the increase in the incidence of the disease which we find to occur as the amount of tuberculosis in the immediate direct ancestry increases.’

Thiele of Dresden brings forward statistics showing that tuberculosis is a professional disease of workers in porcelain factories, and that the longer they are employed the more likely they are to show signs of the disease. He examined 686 workers in a large porcelain factory in Saxony and found that about 5 per cent. showed signs of tuberculosis as compared with the 2 per cent. found by Koelsch in a Bavarian porcelain factory before the war (vide *Medical Science*, 1920, **2**, 226).

Samson emphasizes the close association between prostitution and tuberculosis, which Spillmann of Nancy in 1905 declared was a venereal disease secondary only in importance to syphilis and gonorrhoea. In an examination of 1,300 women under the control of the Berlin police he found that 10 per cent. showed signs of more or less active tuberculosis. The high incidence of tuberculosis among prostitutes is due to bad hygiene, defective housing accommodation, alcoholism, and sexual excess. Although at least two-thirds of his cases were syphilitic, Samson found that with few exceptions syphilis had no appreciable influence on the origin or course of the tuberculosis and that the two infections ran their course independently of one another.

Symptomatology. Under the name of the 'drooping shoulder sign' Rivers draws attention to a physical sign which he says is not mentioned in any British text-book. On the affected side or side of more extensive or older disease the point of the shoulder and nipple are lower than on the other side. The nipple is also smaller and seems to be further back. Muscular atrophy also is noticeable, the pectorals and far more of the upper part of the trapezius being involved. The sign, which Rivers regards as tuberculo-toxic in origin, occurs in descending order of frequency in juvenile hilus cases, third stage cases (Turban-Gerhardt), first stage cases, and second stage cases.

Lemoine maintains that investigation of local tenderness on pressure with the finger in the supraspinous fossa, supraclavicular triangle, and intercostal spaces described by Sabourin in 1910 as a means of localizing tuberculous foci should form part of a routine examination. In 192 cases in which the diagnosis of pulmonary tuberculosis was established by the presence of tubercle bacilli in the sputum, Lemoine found that the supraspinous point was constant, being very tender during the acute stage, less tender at other times, but persisting for a more or less long period even after the auscultatory signs had disappeared. In the axilla and intercostal spaces tenderness on pressure was obtained in half the cases, while in the supraclavicular triangle it was almost as constant as in the supraspinous fossa, being present in about four-fifths of all the cases. According to Ragot, who confirms Lemoine's observations, supraclavicular tenderness is an early sign and tenderness in the intercostal spaces occurs later. Ragot considers that this tenderness is almost specific of a tuberculous process, as he has never met with it in any other acute or chronic disease of the lung, such as pneumonia, asthma, emphysema, or hydatid cyst of the lung. It is also absent in certain forms of pulmonary tuberculosis without glandular involvement in which the lesions remain exclusively central. It is most positive in pleuro-cortical and mediastinal forms and in lesions of the apices. It remains present for a very long time after apparent cure and one must wait for its disappearance before declaring that recovery is established. Its reappearance indicates revival of the process.

Salomon remarks that unilateral cavities often cause adventitious sounds to be heard in the opposite lung which are difficult to interpret, being sometimes so marked as apparently to contra-indicate artificial pneumothorax. X-ray examination is not sufficient to remove all doubt, for like percussion it may show old sclerotic lesions which have no pathogenic relation to the sounds heard. The distinction between propagated and autochthonous sounds according to Salomon can be made as follows: Propagated sounds are chiefly heard behind in the paravertebral, supraspinous and infraspinous regions, and much less frequently in front in the infraclavicular regions. They consist more frequently of rubs than of moist râles. They are absolutely continuous with those which are heard in the diseased lung and become less distinct as one moves away from the middle line. Propagated sounds are never heard in the axilla of the normal side, and are not heard on auscultation of the corresponding supraclavicular fossa. Their extrinsic origin is proved by their usually disappearing after the first insufflation of pneumothorax.

Stephan states that from 1912 to 1919, 476 cases of pulmonary tuberculosis in persons over 40, consisting of 338 men and 138 women, were admitted to the Municipal Hospital for pulmonary tuberculosis at Mannheim.

The influence of the war was shown by a considerable increase in the mortality and by a more rapid course of the disease. According to Stephan, the characteristic features of **pulmonary tuberculosis in advanced life** are the early loss of flesh and anaemia, which may both give rise to erroneous diagnoses, so that an early X-ray examination is desirable, a frequently afebrile course, and a low blood-pressure. Hypertrophy and dilatation of the left ventricle, which are also frequently found *post mortem*, may be the only evidence during life of renal sclerosis.

The morbid anatomy of pulmonary tuberculosis in advanced life was characterized both during and before the war by a tendency to the formation of fibroid tissue, in contrast with the autopsies on younger persons in whom exudative processes predominated during the war. The aggravation of the prognosis of pulmonary tuberculosis in advanced life is therefore not due to a change in the nature of the pulmonary process, but is explained by the diminished resistance of the system caused by circumstances connected with the war.

Pissavy remarks that in old persons especially pulmonary tuberculosis often simulates chronic bronchitis and emphysema. In such cases the general condition is little affected, and the person in question is able to carry on his ordinary occupation, provided certain precautions are taken. Persons of this kind, however, are extremely dangerous to their environment, and are the frequent causes of disseminating tuberculosis while they are supposed to be merely suffering from chronic bronchitis and emphysema. In all cases of chronic bronchitis, therefore, a careful inquiry should be made into the cause of the condition, as apart from gas-poisoning there are only four causes of chronic bronchitis, viz. asthma, lesions of the nasopharynx, renal disease, and cardiac insufficiency. If none of these factors are present, examination of the sputum for tubercle bacilli should be made at least five or six times at more or less distant intervals before tuberculosis can be excluded.

Lortat-Jacob and Turpin studied the course of pulmonary tuberculosis in 30 cases who presented the **arcus senilis**, or corneal ring as they prefer to call it, since it was sometimes present in patients of 45 or even 34 apart from any signs of premature old age. They found that the corneal ring was usually associated with fibrotic forms of pulmonary tuberculosis as distinct from forms with a tendency to caseation, all the cases with two exceptions in which the disease assumed an ordinary fibro-caseous form being examples of chronic fibroid tuberculosis. The prognosis, therefore, of these cases with a corneal ring is that of chronic fibroid tuberculosis, namely, relatively favourable when compared with the rapidly fatal course of extensive fibro-caseous tuberculosis. The writers regard the corneal ring as a sign of the neuro-arthritic diathesis like the camptodactyly, or permanent inflexion of one or more fingers described by Landouzy, which it resembles both in a pathological and semeiological respect. Unlike camptodactyly, however, which is most frequent in women, the corneal ring appears to predominate in men.

McCann and Barr found that the **basal metabolism** of tuberculous patients may be normal or very slightly above that of normal men of the same size, and that further slight increases in metabolism occurred with a rise of body temperature. The basal heat production in tuberculosis was found to be less than the normal for the same patient when in health; in other words, the loss in weight might be accompanied by a reduction in metabolism which more than compensated for the tendency to increase caused by the disease. Limited data regarding the nitrogen excretion showed that though a toxic destruction of protein did occur in tuberculosis it was not large. The specific dynamic rise in metabolism produced in two cases by the ingestion of a protein meal corresponded closely with that produced by the same meal in three normal men. The writers conclude that as the food requirements of tuberculous patients are not large either as regards total energy value or nitrogen content forced feeding is unnecessary and probably harmful in the active stages of pulmonary disease. Since protein increases the respiratory exchange in the tuberculous as in normal persons, the protein intake should be limited while the disease is active in order to put the lungs at rest.

Le Noir and Goiffon examined the stools of tuberculous patients who had a normal or subfebrile temperature without advanced lesions or any clinical signs of enteritis. The results showed that the functioning of the alimentary canal in pulmonary tuberculosis was defective even during the first stage when the stools are apparently normal. There was either an excess of fermentation or putrefaction or a combination of both. The practical outcome of these observations is that one must not depend on the functional integrity of the alimentary canal in tuberculosis, even if it appears normal. Over-feeding should be carefully supervised, and a coprological examination should be frequently made so as to control the diet and prevent the occurrence of enteritis, which is such a formidable complication of this disease. Carbohydrate fermentation can be prevented by restriction of food rich in cellulose. The writers also obtained good results by administration of calcium salts.

Janowski of Warsaw has observed 523 cases of **pulmonary tuberculosis simulating Graves's disease** in patients of different ages. In 75 per cent. of the cases the patients, who were usually women, were suffering from nervous and physical disturbances and complained of sweating, shivering, instability of temperature, sensations of cold, cough, and digestive disturbances. In 22 per cent. of the cases observed in Russia, and in more than half of those seen in Poland, the patients were in a state of profound apathy and fatigue. Lastly, there was an intermediate type presenting alternate attacks of over-excitement and apathy separated by a relatively short normal period. The close relationship between hyperthyroidism and tuberculosis is shown by the fact that Janowski found 510 examples of hyperthyroidism among 3,000 tuberculosis cases. In 80 per cent. of the cases of hyperthyroidism examination of the lungs showed incipient pulmonary tuberculosis. In 10 per cent. the symptoms of hyperthyroidism preceded those of pulmonary tuberculosis by a few months and even by two years, but in half these cases the rays showed the existence of tracheobronchial adenopathy. Lastly, in barely 10 per cent. there was a latent tuberculosis. The prognosis is generally favourable, for in 90 per cent. there are only very slight lesions in the lungs. An early diagnosis is important, as the disease can then be carefully treated. There is a considerable difference between thyreo-tuberculosis or combination of hyperthyroidism and tuberculosis and Graves's disease. While the latter often requires surgical treatment after medical measures have failed, thyreotuberculosis subsides completely and permanently in the great majority of cases without an operation being necessary.

From his observations on 80 **cuti-reactions** performed during and apart from menstruation and a study of the cuti-reaction in 53 women who had undergone unilateral or bilateral ovariotomy as well as from observances on 53 controls, Coulaud came to the conclusion that menstruation and ovariotomy are accompanied by a phase of tuberculin anergy similar to that described by Nobécourt and Paraf in pregnancy (vide *Medical Science*, 1920, **2**, 236–7). On the other hand, Bernard, Salomon and Joannon, who studied the cuti-reaction in 67 women during and apart from menstruation, found that the results were so variable that they concluded that the hypothesis of anergy during menstruation was not justified.

Diagnosis. Peters has carried out Pirquet's test, as modified by Petruschky, in 5,044 patients belonging to Petruschky's private clientèle. Most of these patients consulted Petruschky in his capacity of a tuberculosis specialist, and they could not therefore be regarded as a typical sample of the community. There were 864 negative reactions to the first test, which, in 444 cases, was repeated. This repetition of the test in the negative cases yielded 27 per cent. positive reactions, and Hamburger's thesis is thus confirmed; two successive tests yield a considerably higher proportion of positive reactions than a single test. Reference is made in this connexion to the findings of Nothmann, who in persons under 17 obtained a positive reaction only in 47·1 per cent. to the first test, and in 65·5 per cent. to the double test. Classifying his cases (giving a negative reaction to the first test) according to the age of the patient, Peters shows that under the age of 5, only 11 per cent. gave a positive reaction to the second test. This percentage rose steadily with the age of the person examined, and after the age of 40, 54 per cent. of the persons giving a negative reaction to the first test, gave a positive reaction to the second. Peters' explanation of this phenomenon assumes that in persons over middle age tuberculous foci are often so effectively encapsuled that it requires a preliminary interaction of tuberculin with the skin for Pirquet's test to become positive. There were only 113 doubtful reactions in the 5,044 persons on the first test, and when this was repeated, 82 per cent. gave a definitely positive reaction. The odds are, therefore, that a doubtful reaction to the first test will prove positive on repetition. Grouping his cases so as to include in one category only those without any clinical sign of tuberculosis, Peters shows that among 965 such cases from the age of 6 onwards, 72·2 per cent. gave a positive reaction. An analysis of the Pirquet findings in connexion with enlarged lymphatic glands suggested that, at any rate among young children, this enlargement must often be traced to other causes than tuberculosis.

Carnot and Libert, after having ascertained by the duodenal tube that the tubercle bacillus is present in advanced stages of the disease, investigated the diagnostic value of this method in cases in which the bacteriological proof was not otherwise obtainable. For this purpose seven cases were examined, consisting of four cases of tuberculous peritonitis of the ulcerative or fibro-caseous form without intestinal disturbance, one of Poncet's rheumatism, one of encysted pneumothorax with emphysema and disseminated bronchitis without bacilli in the sputum, and one of cervical and mediastinal adenitis with fever resembling that of miliary tuberculosis. The results were positive in three cases, viz. the one last mentioned and two cases of tuberculous peritonitis. In none of these three cases was there any sputum. In another group of eleven patients in which tuberculosis was probably not present the results were constantly negative. It is thus obvious that the tubercle bacillus may be eliminated by the bile and pancreatic juice even in cases where there are no bacilli in the sputum.

Investigations have recently been made by several observers such as Bressel, Eliasberg and Schiff, and Gibson and Carroll, into the auto-urine test for active tuberculosis described by Wildbolz of Berne in 1919. The test is performed by evaporating 150 c.cm. of the patient's urine to one-tenth of its volume *in vacuo*, and injecting 0·1 c.cm. intracutaneously. If the reaction is positive a local infiltration of the skin results within 18–24 hours after introduction of the fluid. A control urine is injected at the same time. According to Bressel, the reaction appears at an early stage of the disease, so that in doubtful cases it is a valuable help in establishing the diagnosis. If the correct technique is employed, no bad effects occur. The drawbacks to the reaction are that it is painful and the technique complicated and therefore unsuited for general practice. Gibson and Carroll performed the test on 40 children at the Meriden State Tuberculosis Sanatorium, Connecticut, with the following results: (1) All cases with bone tuberculosis reacted distinctly to the test. (2) In none of the cases were there conflicting results. In every case in which there was definite allergy to tuberculosis along with signs of activity the reaction was positive. All the anergic patients with positive signs gave definite reactions when their urine was injected into allergic individuals except in one case of renal impairment. (3) Negative reactions obtained in the allergic cases confirmed the opinion that the individuals had no active tuberculosis. Eliasberg and Schiff, who tested the reaction in 40 children, consider it as worthy of further trial, although their results were not invariably confirmatory of Wildbolz's observations. (Vide also *Medical Science*, 1921, **4**, 559–60.)

Burdick and Gauss have examined the sputums of 191 tuberculous patients, and found the albumin reaction positive in 95 per cent. of patients with incipient pulmonary tuberculosis, in 98·4 per cent. of patients with moderately advanced pulmonary tuberculosis, and in 92·6 per cent. of patients with advanced pulmonary tuberculosis. It was positive in 96·3 per cent. of all the patients. In 6 cases of chronic non-tuberculous bronchitis and in 2 of asthma no albumin was found in the sputum. Examination of the sputum of the same tuberculous patient on successive days showed that albumin was invariably demonstrable. The authors conclude that this test is of great value in distinguishing between pulmonary tuberculosis and other chronic diseases of the respiratory tract.

Stivelman (1) of the Montefiore Sanatorium, New York, twits specialists as well as general practitioners with their mistaken diagnoses, and he has found that, although patients were admitted to his sanatorium only after the original diagnosis of tuberculosis by a general practitioner had been corroborated by at least one specialist, yet in a series of 1,700 consecutive admissions there were as many as 176 (10·4 per cent.) cases which proved, on observation, to be non-tuberculous. The list is headed by chronic bronchitis and emphysema with 32; heart disease with 18; non-specific diseases of the upper respiratory tract with 15; neurasthenia with 15; chronic interstitial pneumonia with 12; bronchiectasis with 10; and chronic non-tuberculous lung infections with 11. This paper is a criticism of diagnosis by a single examination and a justification of diagnosis only after adequate observation.

De Fleury describes a psychopathic pseudo-tuberculosis characterized by wasting, pallor, loss of desire for food, work or pleasure, damp hands, night sweats, tachycardia, general tremor, low blood-pressure, dry cough and impaired resonance at the right apex. The true signs of pulmonary tuberculosis, however, are absent, namely, those furnished by percussion, auscultation and radioscopy, and there is no evening rise of temperature. The cause of the pulmonary insufficiency in these cases, according to De Fleury, is a constant spasm of the respiratory system. He regards the condition as a manifestation of an emotional constitution hitherto more or less latent under the influence of a slight attack of melancholia. The prognosis is favourable, but relapses may occur. Treatment should be directed to calming the restlessness. spasmodic anorexia and insomnia.

Treatment. Klemperer has tested the claims of Schmidt's 'Proteinkörpertherapie', which since 1916 has been applied to almost every known disease. As far as pulmonary tuberculosis is concerned, Klemperer has little good to say of this treatment. In his hospital he has given diagnostic injections of milk in 25 cases exhibiting, or suspected of, tuberculosis. Focal reactions were comparatively rare and indefinite, but in as many as 22 cases more or less fever was provoked. But this could not be regarded as a specific reaction, for in 30 non-tuberculous cases he obtained a general febrile reaction to the first injection in 20 cases, and to the second or later injections in 6 other cases. Only in 6 out of the total of 55 cases were the injections followed by euphoria, and 3 of these cases were non-tuberculous. He also experimented with alternate injections of tuberculin and milk, and he came to the conclusion that the latter was incomparably inferior to the former as a specific agent. His experience of the therapeutic injections of milk was also disappointing; in 6 cases they proved inert, and in 2 directly harmful.

Leichtweiss has treated 30 cases of pulmonary tuberculosis by cutaneous inoculation with tuberculin on Ponndorf's lines slightly modified. The immunizing response of the individual having been determined by Pirquet's test, 2 to 3 small abrasions were made on the upper arm, and a small drop of undiluted old tuberculin was rubbed in with a glass rod. The further dosage was regulated by the local reaction and, in some cases, by a general or focal reaction; but as a rule the next inoculation was undertaken 3 or 4 weeks later, 6 to 10 abrasions, about 3 cm. long, being made on the other arm. A third inoculation would follow in about 4 to 6 weeks at a new spot, and the dosage never exceeded 2 drops of tuberculin rubbed into 10 abrasions. Most of the patients suffered from afebrile stationary disease; marked improvement was effected in 11, and considerable improvement in 8. There was no change in 8, and in 3 the disease progressed. In 9 out of 27 sputum-positive cases, tubercle bacilli disappeared permanently from the sputum. Leichtweiss regards this treatment as a definite advance in tuberculin therapy, and points out that it is simple and particularly suitable for ambulant cases as the intervals between the inoculations are long. But he deplores the comparative inaccuracy of the dosage of tuberculin which its administration through the skin entails.

Luithlen finds that treatment with Deycke-Much's partial antigens in tuberculosis gives rise to definite leucocytosis in all but the most serious cases, even when minute doses are given, and even when there is no rise of temperature. But he finds no prognostic clue in the total number of leucocytes. He believes that this partigen treatment constitutes a considerable stimulus to the lymphatic system which responds by an increased output of lymphocytes in the blood. But again he sees in this increased output no reliable clue to prognosis or treatment. When the injections are well tolerated, and the clinical course of the case is satisfactory, a rise in the number of eosinophils may be observed after each injection, and this rise may be maintained. On the other hand, when the clinical course of the case is doubtful or unfavourable, there is either no rise in the number of eosinophils, or there is an actual fall following a transitory rise. When no reaction follows the injections, and the number of eosinophils diminishes rapidly, the case is not suitable for partigen treatment; and in this respect the behaviour of the eosinophils is a certain therapeutic guide.

For two years Frischbier has been treating pulmonary tuberculosis with inunctions of Petruschky's tuberculin liniment, and his report deals with 88 cases treated in a sanatorium, and 30 given ambulant treatment. He selected for this treatment only those patients he considered capable of an adequate reactive response. The results were good in the sanatorium cases, but Frischbier admits that it is difficult fairly to allot praise for results when these have been achieved by a combination of specific and institutional treatment. Far more instructive were the 30 ambulant cases; in 23 of these there was marked improvement in the general condition, although treatment was practically confined to tuberculin inunctions.

Grossmann's short monograph on Petruschky's tuberculin liniment covers a fairly wide field, and begins with a historical survey of the administration of tuberculin by the skin since this method was first advocated by C. Spengler in 1897. The modifications made since this date are discussed, and special attention is given to the researches which led up to Petruschky's tuberculin liniment treatment. Separate chapters are devoted to the general pathology of tuberculosis, the technique of tuberculin liniment treatment, its indications and contra-indications, and to the literature of this subject. It is not quite clear whether or not this survey of the literature embraces only those publications which more or less endorse the author's own views on the subject. He writes with the enthusiasm of a physician whose conversion to this system is due to his own recovery under it after other and prolonged treatment had failed.

Wernscheid has given the gold salt krysolgan in 17 cases of tuberculosis of the larynx. The drug was given by intravenous injection, the initial dose varied from 0·025 to 0·05 gm., and it was repeated every 8 to 10 days in increasing quantities. In most cases there was both a general and focal reaction, and the results were better in those cases in which fever and other signs of reaction were observed than in those which showed no reaction. Even after only 2 or 3 injections ulcers of the larynx were distinctly cleaner, and there were other objective signs of improvement. In 3 cases the patients' general condition was too desperate to give the drug a fair chance, and in 7 other cases the disease progressed or was stationary. In the remaining cases the results were often amazingly good, even when the disease was far advanced.

Keutzer's verdict as to the value of krysolgan in tuberculosis is favourable in regard to cases of comparatively inactive disease, whereas he finds actively progressive disease to be hastened, rather than checked, by this gold salt. In addition to tuberculosis of the lungs and larynx, he has treated tuberculosis of the wrist and parenchymatous keratitis. By excluding all febrile cases, and waiting till the reaction provoked by an intravenous injection had passed off before giving another injection, he achieved results which he ascribes to the definitely specific action of the drug on tuberculous tissues. He never saw permanent ill effects on pulmonary tuberculosis from this treatment, and such temporary discomforts as slight giddiness and allied symptoms could be traced to a too hasty injection or to the solution being too cold. When some of the solution escaped into the extravenous tissues, the infiltration provoked was not so painful or persistent as is the case with salvarsan.

Hassencamp, of the Halle University Medical Clinic, states that the inquiry conducted by Schwalbe, editor of the *Deutsche medizinische Wochenschrift*, as to the value of Friedmann's remedy yielded the following results. Almost all internists gave an unfavourable reply, many indeed did not think its use justifiable. Paediatrists gave a similar verdict. A few favourable reports were given by surgeons, but most of them were opposed to its use. The successes reported by some writers can be explained in several ways. In the first place, it must not be forgotten that tuberculosis often clears up spontaneously. Secondly, in many instances inactive processes have been treated. Thirdly, in some cases the good result may have been due to the non-specific action of the protein introduced. Hassencamp's personal experience of Friedmann's remedy has been as follows: A true cure was not observed even in mild, incipient, apical disease. Arrest or transient improvement of the disease occasionally occurred, but this is not infrequent apart from treatment. Permanent cessation of fever, cough, expectoration, &c., was never observed. In some cases the injection did not appear to have any effect whatever. Finally, in some instances decided aggravation of the symptoms occurred during treatment. Hassencamp concludes that clinical experience has not confirmed the curative action of Friedmann's method.

Several French writers, such as Amaudrut, Grenet and Drouin (1) (2), Rénon and Rosenthal, speak highly of the metals of the cerium series such as didymium, praseodymium and neodymium in the treatment of pulmonary disease and other forms of tuberculosis. Grenet and Drouin recommend this treatment only for chronic and apyrexial forms, but Rénon has used it in febrile cases with encouraging results. Rénon has found that injection by the intravenous, intrarectal, or intratracheal routes is well tolerated, whereas subcutaneous or intramuscular injections recommended by Grenet and Drouin were so painful that they had to be abandoned. According to these writers the treatment is beneficial partly by its bactericidal action and partly by its causing an intense mononucleosis.

Webb, Forster, and Gilbert recommend postural rest in the treatment of pulmonary tuberculosis. In patients with much expectoration a short time several times a day is allowed to be spent lying on the less-affected lung. The patient then turns on the side of the more diseased organ, beginning with only a few minutes and gradually increasing until 20 hours or more a day are spent lying in this position. The writers state that results are obtained in a few weeks comparable to those obtained more rapidly by artificial pneumothorax, as the fever subsides, the cough ceases, and sputum decreases to a mere trace. Postural rest should be continued for many months after expectoration has diminished or ceased, or the temperature has remained normal, as is the usual procedure in artificial pneumothorax. The greatest benefit is to be derived in cases of unilateral disease. If both lungs are diseased, the most active lung should be rested. If the disease is equally active on both sides, rest on the back is advocated.

The three chief conclusions to which Saxtorph comes after a study of the results of pneumothorax treatment for working-class patients are: (1) permanently as well as temporarily beneficial results can be obtained; (2) working-class as well as well-to-do patients may derive permanent benefit; and (3) a small, incomplete pneumothorax is often worse than useless. The material on which these conclusions are based consists of 200 patients who were admitted to a working-class sanatorium, and whose disease was such as to indicate pneumothorax treatment. Ten years had elapsed since this treatment was instituted in the earliest cases, and thus there was material for gauging the permanency of the results. In 58 cases a pneumothorax could not be induced because of pleural adhesions, in 34 only a partial pneumothorax, and in 108 a more or less complete pneumothorax could be induced. Of the 58 patients in the first class, 35 had died within 2 years, and 12 at a later date. Six were still alive but unfit for work, and only 5 were fit for work 2 years after discharge. The results were still more disappointing in the second class, in which only a partial pneumothorax was induced. Of these 34 patients, a few could not be traced, 27 were dead within 2 years of discharge, only 3 survived this observation period, and of these only 2 were fit for work. Saxtorph suggests that a small pneumothorax does more harm than good because it subjects the lung to stresses and strains which complete immobilization of the lung eliminates. He elaborates this argument by an account of a case in which the X-rays showed a cavity, of the size of a large pigeon's egg, surrounded by densely infiltrated tissues. After the induction of a partial pneumothorax, the X-rays showed the lung to be adherent to the chest wall in the neighbourhood of the cavity, and the progressive enlargement of this cavity under pneumothorax treatment was rapid. With such discouraging results from a small, partial pneumothorax, it is urged that, when adventitious sounds persist and there are other signs of inadequate compression of the lung, pneumothorax treatment should be discontinued.

In the third class, represented by 108 cases, the results of a large pneumothorax were in a comparatively high proportion of cases excellent even after an interval of many years. Altogether 34 patients were still alive 2 to 6 years after discharge, and nearly all of them were fit for work. In other words, 33 per cent. of the patients in this class obtained more than temporary relief from this treatment. A re-grouping of all these patients, according as they were febrile or afebrile when pneumothorax treatment was first attempted, showed that the ultimate prognosis was far better for the latter class.

Saugman states that from December 1906 to August 1920 500 cases were treated at the Vejlefjord Sanatorium in Denmark by artificial pneumothorax. Apart from two cases of sudden death, probably due to gas embolism, no accidents occurred. He has followed up 257 patients who were discharged from the sanatorium between 1907 and 1916, and found that 33 per cent. were fit for work. He regards it as dangerous to interrupt insufflation under a year. In favourable cases, if the pneumothorax was started before induration of the lung, compression may be stopped at the end of a year, but, as a rule, it is best to continue it for two years. In chronic cases Saugman deprecates interruption of pneumothorax, as he has seen relapses occur after three or even four years. When compression has to be maintained for a long period insufflation may be performed every two or three months. When the pneumothorax is complete Saugman keeps it up for about five years, and then, if the patient wishes it, he stops the insufflation, preferably in the summer.

Jaquerod states that in a large number of cases the question of how long an artificial pneumothorax should be maintained is decided by itself, as the lung after a pleural effusion is drawn back into its place by adhesions, or the thorax becomes filled up with fibrinous deposit without its being possible to prevent this occurrence. In 22 cases of this kind observed by Jaquerod the tuberculous process assumed a more or less rapid course after absorption of the effusion, in 5 its course was slightly delayed, in 3 there was considerable improvement which was maintained for 3 or 4 years, and in 2 apparent recovery took place. But if no effusion occurs or the pleural cavity remains full after absorption of the effusion, Jaquerod considers it advisable to keep up the artificial pneumothorax indefinitely to prevent relapses, and sometimes throughout the patient's lifetime.

Bernard and Salomon remark that though one of the classical contra-indications for pneumothorax is the presence of bilateral lesions, it is not always easy to determine that they are bilateral, or, rather, it is not always easy to interpret the clinical or radioscopic signs in the opposite lung to that in which the principal lesions are situated. They record a case in which, owing to the presence of bilateral disease, artificial pneumothorax was not performed, but in which a spontaneous pneumothorax developed to the great benefit of the patient, who, owing to the pneumothorax which was natural at first and later was continued artificially, was on the high road to recovery at the time of publication of their paper.

Stivelman (2) maintains that a bilateral lesion *per se* does not constitute a contra-indication to artificial pneumothorax. In most advanced tuberculosis the lesion is bilateral, but in one lung the disease is comparatively inactive, and after artificial pneumothorax the untreated lung is favourably affected, and the general condition shows decided improvement. Of the last 65 cases treated at the Montefiore Sanatorium 38 suffered from far-advanced bilateral lesions which ran an active progressive course, and their chances for recovery under the ordinary sanatorium care were very poor. Under pneumothorax treatment 4 cases, or 10·4 per cent., were discharged with the disease in the arrested condition; 18, or 47 per cent., made remarkable improvement, many of them being able to resume their work; and the remaining 16, or 42·6 per cent., did not profit by the treatment.

Cassinis also testifies to the value of artificial pneumothorax in bilateral disease from his experience of 17 such cases, in some of which the lesions on the least affected side were slight and early, and in others extensive but not very advanced.

According to Dumarest, Parodi and Lelong the pleural effusions occurring in the course of artificial pneumothorax may assume various forms, which may be classified as follows: (1) Idiopathic effusions, which are independent of any local infection, and are caused merely by the chronic trauma constituted by the presence of gas in the pleural cavity. The effusion is generally early in appearance, scanty in amount, and is rapidly absorbed without leaving any trace. Fever and constitutional symptoms when present are of short duration, but are usually absent. The fluid contains only a little albumin, and is only slightly coagulable. The cytological formula is characterized by eosinophilia and more or less marked lymphocytosis according to the duration of the effusion. (2) Tuberculous pleurisy, the most frequent form, of which there are two types. One is relatively mild and the other severe. In both types the fluid is rich in albumin. The lymphocytosis present at the onset enables tuberculous pleurisy to be differentiated from the idiopathic effusion, the clinical signs not being sufficient to establish a diagnosis. (3) Septic pleurisy always has an acute course with constitutional disturbance and more or less persistent fever. The cytological formula is characterized by lymphocytosis, sometimes polymorphonuclear leucocytosis, and the presence of red cells. The writers' conclusions are as follows: (1) The presence of artificial pneumothorax may play a part in the production of pleural effusion. (2) Certain effusions, which may be called idiopathic, may, at least at the onset, be entirely due to this cause, and their prognosis is always favourable. (3) The diagnosis of the nature of these effusions can be established from the first by their cytological characters. (4) Generally speaking, cytological examination in association with the cervical symptoms furnishes a number of data useful for diagnosis, prognosis, and treatment of the pleural effusions occurring in artificial pneumothorax.

De Reynier and Rossel, of Leysin, remark that though effusion on the affected side is extremely common in artificial pneumothorax, effusion on the 'sound side' is rare, only two examples of the kind having been hitherto reported, by Als and Süssdorf respectively. The writers record two more cases in which, like those of Als and Süssdorf, recovery took place and artificial pneumothorax could be continued. Their conclusions are as follows: (1) Effusion on the 'sound side' in artificial pneumothorax is a complication independent of the treatment, and must be regarded as an ordinary infective pleurisy, probably of tuberculous origin. (2) The appearance of an effusion on the opposite side to the pneumothorax is a grave, but not necessarily fatal, complication in spite of the considerable diminution of the respiratory area. (3) The evolution of these pleurisies is identical with that of ordinary pleurisies. In the writers' two cases the absorption of the effusion was complete in three months, and in neither case did the subjacent lung suffer. (4) Treatment, as in ordinary pleurisy, must be symptomatic at first. If the dyspnoea is very intense the effusion must be evacuated, and, owing to the other lung being out of action, operation will be required earlier than in ordinary pleurisy with effusion. If there is at the same time hydropneumothorax on the side treated by insufflation this side should be evacuated first and the fluid replaced by nitrogen. But if there is only a very small effusion no treatment is required, and the insufflations should only be resumed when the acute stage of the pleurisy on the opposite side has subsided.

Burnand (1) states that if artificial pneumothorax is complicated by pleurisy, however mild and transient it may be, the pleura undergoes a permanent inflammatory change, so that when the two layers come in contact again they are almost bound to become adherent to one another. This symphysis appears to be inevitable whatever treatment is adopted, even if the fluid has been evacuated by puncture or absorbed spontaneously. The union of the two layers does not take place immediately, and if one intervenes during the period when the rub is audible, which usually does not exceed a month after the two layers are brought together, the layers may be separated and pneumothorax reconstituted. In cases where artificial pneumothorax has not been accompanied by any obvious pleurisy, the pleura may remain separate when brought into contact again. This, however, is only likely to occur when the trauma has been insignificant and transient, which is never the case in artificial pneumothorax which has lasted some months.

Out of a total of about 300 cases of pneumothorax Burnand (2) has met with 14 examples of perforation of the lung. The perforation may be wide or narrow, temporary or permanent, exogenous or endogenous, and give rise to a valvular or open pneumothorax. The exogenous causes are perforation of the pleura and parenchyma by the needle and perforation by rupture of a pleural band. Endogenous perforations are due to extension of an intrapulmonary ulceration process giving rise to a narrow or wide perforation of the visceral pleura. In temporary perforation the essential features are as follows: (1) The perforation is narrow and tends to become obliterated if the patient survives. (2) The initial symptoms are generally intense and sudden. (3) The manometer shows that the pressure of gas rises and keeps high in the pneumothorax cavity. The pneumothorax is valvular or closed from the first. (4) The danger is due to asphyxia rather than to pleural complications. (5) The subsequent pleurisy is serous or purulent, but rarely very septic. (6) The prognosis is bad, but not fatal. (7) Treatment consists in removal of a moderate degree of gas as late as possible, or better still in insertion of a permanent tube. In permanent perforation, on the other hand, the perforation is large and definitive, its onset is insidious, the intrapleural gas pressure is in constant equilibrium with the intrabronchial pressure in spite of insufflation of gas into the thorax, the danger is due not to asphyxia but to the pleurisy which is always purulent, tuberculous, and septic; the prognosis is fatal, and treatment consists in immediate pleurotomy.

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MEASLES

Epidemiology. Cumming (1) states that in 1918 there were four times more measles per thousand among the American troops in the United States than among the American Forces in France. On the other hand, in the United States there were half as many deaths per thousand cases as in France, where there were 42·6 deaths per thousand cases as compared with 23·7 per thousand cases of measles in the United States. Cumming attributes the difference in the two death-rates not to a greater virulence of the measles virus but to the greater frequency of complications due to healthy carriers among the troops in France. He regards the so-called ‘virulence of measles’ as determined by the pneumonia healthy carrier rate. Although recruits, owing to their greater mass susceptibility, were more prone to measles, seasoned soldiers with their higher pneumonia carrier rate were more prone to the complications of measles which caused the fatalities. Only 2 per cent. of the total deaths attributed to measles in France were uncomplicated, pneumonia being almost wholly responsible for the remaining deaths. In a subsequent paper Cumming (2) gives tables showing that as the percentage of recruits in the camps decreased, and the percentage of seasoned soldiers increased, there was a corresponding rise in the complication rate. Camps having the highest percentage of recruits had the lowest complication rate, while those having the highest percentage of seasoned soldiers had the highest complication rate.

According to Apert and Vallery-Radot, during 1920 642 cases of measles were admitted to the Hôpital des Enfants Malades in Paris. 558 were discharged cured, the mortality being 13·08 per cent. Although this figure is high compared with the mortality from measles in private practice or in private hospitals such as the Hôpital Pasteur, where it is hardly ever above 4 to 5 per cent.. it compares favourably with the death-rate in the children's hospitals of the Assistance Publique, where it varies from 15 to 20 per cent. In previous years the mortality in the old measles pavilion at the Hôpital des Enfants Malades had been much higher, viz. 33 per cent. in 1898, 25 per cent. in 1899, and 23 per cent. in 1900, while in some years it had been as high as 48 per cent. A great improvement had thus been effected by the opening of a new measles pavilion. 118 cases among those admitted in 1920 were complicated by broncho-pneumonia, which in 72 cases was present on admission and in 46 developed later. Of the 72 cases 52 died—a mortality of 79·16 per cent., and of the 46 cases 22 died—a mortality of 47·82 per cent. The great majority of fatal cases were in children under two years or in those suffering from concurrent whooping-cough and measles.

Morawetz reports an epidemic of measles which occurred in Vienna between November 1919 and February 1920. In spite of the malnutrition and sickly condition of the children, more than a third of whom were suffering from rickets or tuberculosis, the epidemic did not differ from previous outbreaks as regards the number or age distribution of the fatal cases. Of 491 cases admitted to the infectious department of the Francis Joseph Hospital 52 died—a mortality of 10·6 per cent. Of 172 children under 3 years of age 32 or 12·8 per cent. died, while among children of 4 years and upwards the mortality was 6·2 per cent. Two-thirds of all the fatal cases occurred before the end of the third year of life.

Rice reports an epidemic of 177 cases of measles at an Indian agency in the northern part of British Columbia. The disease ran the regular course in so far as the catarrhal symptoms and eruption were concerned, but with greater severity among Indians than among whites, seven of whom were affected at the same time. Age seemed to play no important part in the manifestations of the disease, the age limits being from 2 to over 80, with fully four-fifths of the cases among adults. Catarrhal pneumonia developed in one case with fatal results, being the only death in adults during the epidemic.

As the result of his observations on an outbreak of 14 cases of measles in the Infant Department of the Cologne University Children's Clinic, Baur (1) comes to the conclusion that the disease was contagious only during the catarrhal period and first day of the eruption, the greatest danger of infection being in the transitional stage between the prodromal and eruptive periods. 24 hours after the appearance of the eruption the infectivity of the disease completely disappeared.

Symptomatology. Lewy has made observations on the length of the *incubation period* in 46 families in which there were 71 cases of measles. He found that the most frequent incubation period was 10 days, and the next most frequent 9, 11, and 8 days. In 5 cases it was 14, 15, 16, 18, and 19 days respectively.

Prolongation of the ordinary incubation period in measles by the co-existence of intercurrent infections is illustrated by Baur (2), who records six cases in which the duration of the incubation period ranged from 15 to 17 days owing to the co-existence of scarlet fever or chicken-pox.

In a paper on *repeated attacks of measles*, Salzmann, of the Munich University Children's Clinic, has collected from literature 36 cases in which not only the second but also the first attack was seen by the same observer or by some authentic witness. The following facts are to be learnt from a study of those cases: (1) The relative frequency of a third attack. It might be supposed that, since second attacks of measles are so rare that some eminent clinicians have never seen them, third attacks would hardly ever occur. Salzmann, however, was able to find 21 examples of third attacks of measles on record, and two of a fourth attack. The explanation offered is that if a person does not gain immunity from the first attack, he is not likely to gain it from a second or third. (2) The frequency of a second or third attack of measles occurring in several members of the same family. (3) The absence of anything characteristic in the prodromes, symptoms, course, or termination of a second attack of measles.

An undoubted example of two successive attacks of measles in the same child has since been reported by Lewy, who, as the patient was his own son, had the opportunity of observing both attacks. The first occurred at the age of 2¾ years, and the second, which was equally typical, three years later. The diagnosis of rubella could be excluded, as the boy had a definite attack of this disease three years after his second attack of measles.

Weill and Gardère remark that *acute myocarditis* is very rare in measles. They record a fatal case in a very fat youth aged 16, weighing 60 kgm., in whom, in addition to bilateral broncho-pneumonia, the autopsy showed a typical acute myocarditis in which, as in diphtheritic myocarditis, the interstitial lesions predominated. Owing to the rarity of myocarditis in measles, the writers suggest that obesity, by overloading the myocardium with fat, rendered it more vulnerable.

Thorp records a case of *gangrene of the left leg* which occurred on the eleventh day of measles complicated by broncho-pneumonia in a girl aged 4½ years. Death took place on the fifteenth day. There was no autopsy. Thorp has not been able to find any other case on record, but reference may be made to a similar case reported by Galop, in which gangrene of the right foot and part of the leg developed shortly after the onset of measles complicated by broncho-pneumonia in a female infant aged 19 months, and was attributed to acute arteritis. Five cases of gangrene of one or more limbs following measles were also collected by Barraud in 1904.

Petroselli reports a fatal case of *mediastinal and subcutaneous emphysema* following measles, which he states is the thirty-second example of this complication on record. The patient was a child aged 3 years, who developed the emphysema in convalescence from severe measles complicated by bilateral broncho-pneumonia. The case confirms the gravity of subcutaneous emphysema in measles, especially in the first years of life, death taking place three days after the appearance of the complication, which Petroselli attributes to rupture of the emphysematous alveoli as the result of increased pressure due to certain areas of the lung being consolidated and impervious to air.

According to Box, who reports a case of *acute ascending paralysis* in a girl aged 14, occurring as a complication of measles and ending in recovery, in cases of this kind recovery seems to be the rule rather than the exception. The cord inflammation was evidently either toxaemic or infective in character, and from the dissociated nature of the accompanying anasthenia the lesion was presumably situated in the central grey matter.

A case of *abscess of the right frontal lobe* secondary to emphysema of the frontal sinus, occurring in measles, is reported by Monteleone. Recovery followed operation.

Lereboullet, Marie, and Brizard, examined *Schick's reaction* in 110 cases of measles in children aged from six months to thirteen years, and found the reaction positive in 59 and negative in 51. Classification of the positive reactions according to the patients' ages showed that there were about 60 per cent. between six months and five years, and 40 per cent. between six and twelve years—figures which correspond to those of previous statistics. Measles therefore has no influence on the Schick reaction, which thus differs from other biological reactions, especially the tuberculin cuti-reaction, on which measles exercises an inhibitory effect.

Weill and Bocca, of Lyons, record an epidemic of measles which occurred in a crèche containing children under two years of age exclusively to illustrate the *immunity* of infants under six months to the disease. Of the 33 children in the crèche the 22 who contracted the disease were all over six months, while the 11 who escaped were below that age, the chances of infection being the same for all. In the rare instances in which the new-born or infants within the first few months of life contract measles, the attack is usually mild, as is shown by the cases recently reported by Schulze and Ugón. Schulze's case was a breast-fed infant whose mother had an eruption accompanied by catarrh 14 days before its birth. On the fourth day of life the infant had a morning temperature of 100·4, and an evening temperature of 101·2, and took the breast unwillingly. Apart from rhinitis nothing abnormal was noted. On the fifth day the morning temperature was 102, the evening temperature 101·6, and there was well-marked coryza. On the sixth day the whole body was covered with a typical measles eruption. The following day the rash began to fade, and five days after the onset the temperature was normal. Schulze alludes to a similar case reported by Mairinger, in which the mother gave birth to an infant while her measles eruption was still present. Although the child was isolated directly after birth, it developed a typical measles eruption 14 days later. The infection in Schulze's case occurred *in utero*, and in Mairinger's case at the time of birth. In the three cases reported by Ugón, of breast-fed infants aged from one to two months who were infected by their nurses, the infants all had remarkably mild attacks in spite of the severity of the disease in the nurses. Nassau attributes the relative immunity to measles in the young infant not to a congenital supply of immune bodies, which does not really exist, but to the inability of the cells at this age to furnish the necessary conditions for the development of the disease. He points out that the practical importance of these abortive attacks lies in the fact that the infants may be carriers of infection without presenting the typical picture of the disease.

The recent studies of Blake and Trask on the susceptibility of monkeys to measles and the symptomatology of the experimental disease in these animals have already been noticed (vide *Medical Science*, 1921, **4**, 354–5).

Prophylaxis. Prophylactic injection of children exposed to infection with the serum of patients convalescent from measles, a method introduced by Nicolle and Conseil in 1918, and by Richardson and Connor in 1919, has recently been employed by Degwitz, assistant at the Munich University Children's Clinic, who records his observations in two papers but without any allusion to the work of his predecessors. In his first paper he reports that 25 children so treated who had not had measles all escaped an attack, whereas others who were exposed to the same source of infection and were not so treated contracted the disease. In a subsequent paper he reported that 172 children who had received prophylactic injections between the second and sixth day after infection were without exception saved from an attack, whereas injections given at a later date (seventh to eleventh day after exposure to infection) did not prevent the disease appearing or diminish its intensity. He recommends that the donors should be healthy vigorous children above the age of 3 years who have had an uncomplicated attack of measles. A history suggestive of syphilis or tuberculosis should render them ineligible. He states that children up to the age of 5 years can have 60 c.cm. and above that age 70–80 c.cm. withdrawn without any ill effect. 2 c.cm. of the serum is tested with the Wassermann reaction and if a negative result is obtained three such sera are mixed together. Degwitz's method has been employed by numerous other German clinicians in children's hospitals on a large scale, such as von Torday of Buda Pesth in 261 cases, Kutter of Berlin in 145 cases, Manchot and Reiche of Hamburg in 216 cases, Zschau of Nuremberg in 37 cases, Glaser and Müller of Berlin in 7 cases, and Rietschel of Würtemburg in 7 cases. The results appear to have been generally satisfactory, the cases injected either escaping the disease altogether or having only mild or abortive attacks. Some of the writers, such as Degwitz and Glaser and Müller, recommend that special serum centres should be established in municipal hospitals, where the serum of measlesconvalescents could be provided for use in kindergartens and infant homes. It appears to be specially indicated in cases where measles is particularly dangerous, viz. in children up to four years of age, especially those suspected to be tuberculous, in pertussis, and in florid rickets. Failures are attributed to the serum having been used too late owing to inability to determine the exact date of exposure to infection, as in some of the cases reported by Kutter, Manchot, and von Torday.

As regards the duration of the immunity conferred, Zschau estimates that it is three or four weeks, and von Torday states that two children who had received prophylactic injections subsequently developed measles, one after 75 days and the other after 72 days. The principal drawback to the method, as Kutter points out, is that donors may sometimes not be available, and Rietschel declares that many parents would object to their children serving as donors.

Inasmuch as 98 per cent. of the mortality attributed to measles is due to complications incident to the healthy carrier state, Cumming regards it as imperative that adequate sanitary protection—pasteurization of eating-utensils and hand-cleanliness—be afforded to block the main avenues of transmission of the potentially dangerous group of pneumonia-producing organisms.

Treatment. Rice found that calcium sulphide in half-grain doses caused prompt relief of the catarrhal symptoms and cutaneous irritation, and apparently shortened the course of the disease, lessened the severity of the symptoms, reduced the temperature, and decreased the liability to complications and sequels.

Injections of pilocarpine in cases of oedema of the glottis secondary to measles are recommended by Arrigoni, who urges that they should always be employed before intubation or tracheotomy. In cases of cardiac weakness the injections of pilocarpine should be accompanied by the use of cardiac tonics.

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J. D. R.

PACHYMENINGITIS HAEMORRHAGICA INTERNA (CHRONIC SUBDURAL HAEMORRHAGE)

This condition has been recognized by morbid anatomists for many years, but its causation and the nature of the primary lesion remain the subject of diverse and conflicting opinions. At present two hypotheses compete for acceptance, (1) that haemorrhage is the primary lesion and is followed by organization of the clot, or (2) that the lesion is primarily inflammatory, a pachymeningitis, and is followed by organization of the serous exudate which becomes richly supplied with new and fragile blood-vessels, from which haemorrhage subsequently occurs. But many difficulties remain unsolved by both these hypotheses, and those who uphold them agree in being equally obscure in their statements as to the part played by head injuries, the source of 'primary haemorrhage' and the relation of subdural haematoma to the pachymeningitis, while those who believe inflammation to be the primary lesion tell us nothing as to the causes of the inflammatory process. Oppenheim, who sums up the position in his text-book of nervous diseases, does not make it clear whether he regards traumatic subdural haematoma and pachymeningitis haemorrhagica interna as largely synonymous terms, or as indicating distinct conditions. Apparently he believes that while traumatic subdural haemorrhage may lead to pachymeningitis, yet the latter is not necessarily a sequel of the former; indeed, he says it is 'an accidental affection' in the course of certain chronic inflammatory diseases of the brain which lead to cerebral atrophy, such as general paralysis, senile dementia, or chronic hereditary chorea. Also, it may be a 'primary disease' as when it occurs in chronic alcoholics and in the subjects of certain blood diseases. He regards syphilis as a rare cause.

At the International Congress of Medicine in 1913, in London, Pierre Marie, Roussy, and Laroche reported the results of an extensive pathological and experimental study of pachymeningitis haemorrhagica interna. Their human material was obtained from 49 cases, the majority of which were only diagnosed as such after death. During life the patients had suffered from various nervous diseases without clinical evidence pointing to pachymeningitis. Macroscopically, they differentiated three forms of the condition:

(1) **An arborescent form.** Here a more or less gelatinous exudate covers a variable extent of the convexity of both hemispheres. It is finely penetrated with a network of arborizing new blood-vessels, which may be diffuse in their distribution or in discrete areas. The overlying dura is slightly thickened. In some cases—gelatinous type—the exudate is rough and villous on the surface and ill-defined in outline and free from the darkly-stained brownish colour of the majority of cases. In yet other examples—fibrous type—there are signs of organization into membranes of the periphery of the exudate. These new membranous formations are richly vascularized.

(2) **Haemorrhagic form.** The haemorrhages may be petechial, diffuse, or encysted. In every instance the condition is bilateral. The petechial cases show a thin exudate on the inner surface of the dura which is thickly spotted with small reddish areas of haemorrhage. In the diffuse cases, the dura is lined on its inner surface by a thin layer of darkly-stained gelatinous exudate. The encysted cases may be flattened, or rounded and forming a distinct tumour mass which compresses and deforms the subjacent brain. In both types, layers of 'inflamed dura' surround and enclose the clot and dark tarry fluid of the mass. The enclosing layers are often stratified.

(3) **Ochreous form.** Most of the cases are bilateral. The inner surface of the dura shows a single large, or several smaller, coppery plaques of thickened membrane.

The authors conclude that in every instance the essential feature of the condition is a new formation of vascularized inflammatory tissue. Any condition causing venous congestion of this gives rise to haemorrhage from the fragile vessels which supply it with blood. Therefore, while haemorrhage may be 'primary' in the clinical sense, yet pathologically, inflammation of the meninges is the primary lesion.

Their attempts to reproduce the condition experimentally did not give conclusive results. They injected subdurally in different species of mammal, rabbit and dog—one or more cubic centimetres of blood—either sterile non-defibrinated blood, blood infected with staphylococci or mixed with irritative substances such as fatty acids and sodium nucleinate. Only in the last instance did a slight non-haemorrhagic meningeal reaction develop, and they conclude that haemorrhage alone is not sufficient to account for pachymeningitis haemorrhagica in man but a microbial or chemical irritation is also essential. How either arises in man they do not indicate.

Since the pachymeningitis in their cases was for the most part diagnosed for the first time at post-mortem, it follows that they had no information as to the duration of the process. Therefore, we cannot decide whether their 'forms' of the condition are really such or are not rather different stages in the development of a single and fairly uniform pathological process. In short, one cannot but suspect that the classification is arbitrary and purely conventional, and gives no clear idea of the causation or development of the terminal morbid conditions they describe.

In a recent paper, Büdinger comes to a somewhat similar conclusion to Marie, Roussy, and Laroche from clinical observation. His chief preoccupation is to account for the sudden development of delayed symptoms of cerebral compression so characteristic of the condition ('Spätapoplexie'). Since the experiments we have quoted completely ignore the fundamental time factor they naturally give us no information on this point.

Like the other views which he criticizes, Büdinger's conclusions are still largely speculative and leave the final solution of the clinical and pathological problems of subdural haematoma and pachymeningitis haemorrhagica interna unsolved. It is therefore a pleasure to turn to another discussion of the question, which is based upon sound principles of cerebral pathology, carries the problem farther than any of its predecessors, and makes less demand upon faith than any of them. In a paper published in 1914, Trotter emphasizes the primary importance of the time factor in determining the symptomatology of a nervous lesion. He points out that the majority of progressive lesions produce their effect upon the brain through interference with its circulation rather than by destruction of its substance. In the case of head injuries, haemorrhage and oedema are almost exclusively the causes of the disturbances of cerebral functions, and they produce their effect by compressing the vessels and limiting the circulation in the parts affected. It is because these effects are thus produced that the rate of development of the lesion exercises so remarkable an influence upon the disturbance of function resulting. Subdural haemorrhage illustrates the variety of clinical manifestations which is produced by lesions developing at different rates. While a subdural haematoma may cause profound compression of the brain, it may not be even suspected during life. In the case of rapid compression of the brain from extracerebral traumatic haemorrhage, Trotter traces three stages:

(*a*) **Stage of physical compensation.** When bleeding begins it must displace some of the intracranial contents, and these the fluid contents. The fluids first displaced are those least resistant, the blood in the veins and the cerebrospinal fluid. The displacement of the cerebrospinal fluid can produce no local symptoms, while the venous outflow will not be interfered with until the total venous capacity is reduced below that for the arterial blood. Up to this point the haemorrhage is latent.

(*b*) **Stage of venous congestion.** As soon as the capacity of the veins is reduced below that necessary to carry off the blood reaching the part, venous engorgement results, and the physical compensation of the first stage breaks down. If such a state of venous congestion be rapidly produced it gives rise to increased excitability of the nervous tissues which is manifested clinically by so-called 'irritative symptoms', twitchings, convulsions, delirium, alterations of reflexes, irritability, and restlessness.

(*c*) **Stage of capillary anaemia.** Further increase of the abnormal pressure from continued haemorrhage will now displace the fluids under higher pressures, that is, the blood in the cerebral capillaries. Anaemia of the affected part is thus produced, and results in paralysis of function.

These, then, are the stages in rapid compression of the brain. When the compression develops very slowly the process is modified, though the stages are the same. The new phenomenon seen in these circumstances is a physiological toleration of the venous congestion, so that while anaemia must necessarily produce paralysis of function, congestion does not give rise to irritative symptoms. This is a process of physiological compensation different from and more important than the purely physical compensation with which we have dealt above. Hence it is that a slowly developing subdural haemorrhage may give rise to no definite symptoms until complete anaemia is established. When the margin of toleration is being reached, a very slight increase of compression will suddenly call forth well-marked paralytic manifestations. Even normal variations of intracranial tension may be adequate to pass the limit of toleration, so that the patient suddenly passes into a state indicating severe compression, and as suddenly returns to normal. Such relatively sudden and wide variations in the symptomatology are characteristic of chronic subdural haemorrhage.

As a preliminary to the discussion of pachymeningitis haemorrhagica interna, and before attempting to establish its relationship with **chronic subdural haematoma,** Trotter describes the symptomatology of the latter condition.

He defines it as a collection of blood, often very large, situated between the dura and the cerebral hemispheres, and enclosed within a distinct membrane which appears to have been derived from coagulated blood. It is of traumatic origin. Clinically, it runs a long course of at least several weeks, this course being divisible into a prodromal period and a period of severe symptoms.

Pathologically, the haemorrhage is situated over the convexity of the hemispheres Its longest diameter tends to be antero-posterior, and transversely it seldom extends beyond the Sylvian fissure. The bulk of the mass lies beneath the frontal and parietal bones. In thickness its maximum bulk is about from one to one and a half inches. The blood is encapsuled in a membrane of very characteristic appearance, which is usually thickest externally and may be as much as a quarter of an inch in thickness. It is but slightly adherent to the dura and may be easily stripped off from this. Its surface shows vascularization from the periphery and is variously coloured from altered blood. The inner surface is roughened from adherent clot, while the membrane itself is laminated and often fibrinous. The inner surface of the cyst as it lies against the pia-arachnoid is much thinner and softer, and is slightly adherent to the brain. The contents of the cavity may measure many ounces and consist of a greenish fluid with particles of decolorized clot, or of dark tarry blood, partly fluid and partly clotted. There are no signs of inflammation and no adhesions surrounding the cyst.

Source of the haemorrhage. From the slowness of its course and the insidious onset of symptoms there can be little doubt that the bleeding is of venous origin. It is almost certain that the veins passing from the surface of the brain to the superior longitudinal sinus are the source of the blood.

These short trunks are relatively unsupported, their cranial end is firmly anchored to the sinus, while the other end is attached to the relatively movable hemisphere, and between the two the vein passes without any tortuosity to allow for movement of the brain. We know that considerable movement of the brain is possible as a result of external violence. A history of head injury is rarely prominent in such cases, but it must be remembered that severe injury cannot be expected to cause the kind of lesion required to produce slow oozing of blood from the rupture of one or two delicate veins. On the other hand, Trotter points out that comparatively slight violence favourably directed to produce an adequate displacement of the brain, and nothing else, would give the necessary conditions. Anteroposterior movement is most likely to do this, and therefore a slight blow on the front or back of the head is probably the commonest cause.

The clinical features. There is almost always to be obtained some history of a fall on the front or back of the head. Often so trivial to all appearance as not to have attracted much attention. The prodromal symptoms usually follow after a free interval of a week or so. Headache and mental changes are the most constant of these. The headache is apt to to be severe and persistent, and may be referred to the site of injury. Gradually, sleepiness, apathy, and absent-mindedness develop, and ‘fainting attacks’ occur. Irritative symptoms, so-called, are usually absent. At this stage neurological examination is commonly negative, and often syphilis or some mental disorder is erroneously diagnosed. When this stage has lasted for about six weeks **the period of severe symptoms** develops suddenly. The most important change is an impairment of consciousness, with violent headache and vomiting. This stupor or coma is subject to sudden and remarkable variations, and this fact is of the greatest diagnostic importance. Focal symptoms are often absent, and when found are apt to be transient, elusive, and equivocal. The condition being bilateral makes their recognition still more difficult. Evidence of compression of the motor cortex is the most common. Hemiparesis, rigidity, bilateral absence of the abdominal reflexes and Babinski plantar responses, and localized twitching of a limb or segment of a limb are often seen. A definite epileptiform fit is rare. Speech affection may be observed, and double optic neuritis is frequent. All these physical signs are inconstant and fleeting. Once established, however, recovery from the condition does not occur without operative relief, and the patient’s condition grows steadily worse.

Pachymeningitis haemorrhagica interna. Trotter remarks that this clinical picture is identical with that described by Oppenheim and others as typical of pachymeningitis haemorrhagica interna, and he believes that the pathological finding described as occurring in each of his six personally observed cases is also that of the latter condition. In each of his cases, the encysting membrane appeared to have been derived from the outer layers of the clot, which had organized. It seems as if the clotting is consequent upon the contact of the blood with the brain, the meninges, and cerebrospinal fluid, and that when once the encircling membrane is formed the tendency to coagulation within it is checked. The fluid character of the cyst contents allows for the continuance of the slow oozing from the ruptured veins, for their opening into fluid would delay or prevent thrombosis. In this way the encysted haemorrhage would remain in communication with the veins, and when the venous pressure rose sufficiently, from any cause, to overcome the resistance of the enclosing capsule there would be a slow recurrence of bleeding.

Discussing the aetiology of pachymeningitis haemorrhagica as defined by Oppenheim, Trotter observes that there is no evidence of any special disease of the veins in the various conditions with which it is associated which would lead to rupture. On the other hand, senile dements, patients with chorea, general paralysis, and alcoholism are the very individuals most subject to falls, and least likely to remember the details of their mishaps. Since trivial head injuries are the ones calculated to produce chronic subdural haemorrhage, the absence of a definite history in such patients has no positive value, while the mental changes often resulting from the haemorrhage may be erroneously regarded as preceding the fall in question and therefore still further obscure the issue. Therefore Trotter concludes that: (1) Internal haemorrhagic pachymeningitis is a term which involves an unjustified hypothesis, and should be discarded in favour of some such term as chronic subdural haemorrhage. (2) Apart from certain cases occurring in diseases which cause a strong tendency to spontaneous haemorrhage, and possibly including them, haemorrhagic pachymeningitis is almost if not quite invariably a true traumatic haemorrhage coming from veins torn in their course between the brain and a dural sinus. (3) Haemorrhagic pachymeningitis, being a purely traumatic lesion without an underlying basis of disease, should always be dealt with surgically, and (4) the variable and capricious course of such chronic haemorrhages, far from rendering diagnosis exceptionally difficult, is capable of exact interpretation in accordance with the principles of cerebral pathology, and constitutes a clinical type at once well marked and characteristic.

The treatment on surgical lines presents no technical difficulties. Trotter recommends evacuation through the temporal fossa, using a small osteoplastic bone-flap. If the brain expands well, drainage is not necessary or desirable. In bilateral cases the second side should be opened immediately after the first, without any interval.

Not only has this admirably lucid account a sound clinical and pathological basis, but the train of events described as occurring is in strict accordance with what is known of the pathology of head injuries, and of the functional disturbances resulting from interference with the cerebral circulation. The inflammatory theory has no very convincing pathological basis. The organization of clot cannot rightly be regarded as an inflammatory process, but rather as a process of repair. There is no evidence of any special lesion of cerebral veins in the various brain diseases often associated with pachymeningitis haemorrhagica interna such as would be calculated to explain rupture apart from trauma, while the theory of repeated haemorrhage from the new-formed vessels of the cyst wall equally lacks foundation. We are left, therefore, with trauma and haemorrhage as the fundamental causes, and from this point the sequence of events as described by Trotter is comprehensible and reasonable.

From what has been said, it becomes clear that Marie, Roussy, and Laroche's experiments were extremely artificial and in no single way reproduced the pathological processes at work in man. The time factor was completely ignored and the survival periods of their animals was a matter of days or of weeks at most. The negative results obtained were only to be expected and indicate nothing except a failure on the part of the experimenters to understand the nature of the problem they were attacking.

As Trotter aptly remarks, the clinical neurologist is so exclusively preoccupied with the anatomical problems of localization of disease that he neglects to consider the physiological problems involved, and in this respect these experimental observations are typical of much modern neurological thought. The fallacy that the site of a lesion is of infinitely greater importance than its nature and mode of development has long obsessed the neurologist and has recently been elevated to the rank of an axiom of prime importance, though the protean manifestations of epidemic encephalitis should have done much to expose its limitations. Not only in the light it throws upon a particular problem of neuropathology is Trotter's paper valuable and inspiring, but also because it indicates that clinical neurology is at last endeavouring to throw off the exclusive domination of anatomy. Not until anatomy takes its place beside physiology as one of the servants of clinical neurology, instead of being its sole master, can we hope to see the solution of the many problems of neuropathology which have so long defeated us.

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F. M. R. W.

THE RELATION OF BLOOD COAGULATION TO PURPURA AND HAEMOPHILIA

The sequence of events from the shedding of blood until its coagulation forms a series of physico-chemical phenomena which are not yet fully understood. When blood is shed and comes in contact with a foreign surface, two changes may occur; first an alteration in the blood-platelets, which lose their shape and individuality, and second, there is probably a disturbance of the physical relationships of the colloid elements concerned in coagulation. It is also possible that the change from intravascular to extravascular conditions may play a part in the procedure of clot-formation as suggested by Bloch. The liberation of the primary agent in the clotting process is caused by lysis of the blood-platelets, and their importance in coagulation has been demonstrated clinically and by laboratory experiment. Duke has shown that in purpura the tendency to bleed runs parallel with the decrease in the number of platelets; retractility of the clot, dependent on the presence of platelets, is also deficient in this condition. Experimentally, Le Sourd and Pagnier have produced lesions in animals very similar to those of purpura by the injection of antiplatelet sera, a method of investigation pursued by Ledingham and Bedson. Stahl has confirmed Duke's work on purpura; he finds that injury to the vessel walls is essential in all conditions; that there is very frequently a diminution of platelets, an absence of retractility of the clot, and a diminished viscosity of the blood, these last two factors being regarded as equal in importance to the platelet deficiency. He also finds that the amounts of calcium and fibrin in the blood bear no relation to purpura. Weil has grouped together a large number of conditions exhibiting haemorrhagic tendencies as 'la dyscrasie endothelio-plasmatique chronique haemorrhagique', though more recently he has reclassified them under the name 'hematogenie'. The cases are divided into two groups, one in which haemorrhagic crises alternate with periods of apparent normality, and a second in which some haemorrhagic symptom is always in evidence. The characteristic blood changes are deficiency of platelets, lack of retractility of the clot, and a prolonged bleeding time, though, as in purpura, coagulation is normal. In addition there is lack of resistance of the capillary walls, so that pressure gives rise to petechial haemorrhages in the hyperaemic area. The chief conditions falling under this head are chronic purpuric or petechial states, the 'tendency to bruise', spontaneous haemorrhages from visceral mucous surfaces, and the large group of genital haemorrhages occurring in women typified by menorrhagia, excessive post-partum bleeding, and metrorrhagia at the menopause. In this group he considers that the occurrence in some cases of phlebitis or phlegmasia is sufficient evidence of a weakness of the vessels. There seem hardly to be adequate grounds to warrant the grouping of these genital cases with true purpura.

Purpura therefore constitutes a failure of coagulation in which there is deficiency of blood-platelets, but without lack of the substances essential for clot formation, since coagulation time is normal. Duke considers that the coagulating agent, thrombokinase, derived normally from the platelets, is present in a form which precludes a sufficiently rapid union with calcium salts; bleeding time is thus prolonged as the outflowing blood removes the coagulating agents before they can react, but under the stable conditions of coagulation-time estimation the necessary reactions occur normally. A review of recent work on the purpuras has been published by Mouzon.

In haemophilia the platelets and bleeding time are usually normal, but coagulation time is delayed. There is here a quantitative lack of thrombokinase, as contrasted with the qualitative deficiency in purpura. The aim of treatment in both these cases is to cause a production of normal kinase. Transfusion, direct or indirect, will almost always arrest haemophilic bleeding, but it does not alter the underlying condition, and its effect rapidly passes off. Dufour and Le Hello, following the observation of Richet and Besredka that hypercoagulability occurs during anaphylaxis, were able to control severe haemorrhage by injecting the sera of anaphylactic animals. The immediate results of this treatment were satisfactory, but the duration of the period of hypercoagulability is not stated; such evidence as is given does not indicate that it lasts for long. Vines found that after sensitization of the patient to serum, the induction of a localized anaphylactic reaction caused a decrease in the coagulation time of haemophilics, which lasted as long as the patient would respond to the test for anaphylaxis, a period varying with individuals. Injections of serum form the most common method of treatment in haemophilia, and Weil claims excellent results; Chalier maintains that the most successful form of treatment is the intravenous injection of maternal serum, thus avoiding risk of anaphylactic manifestations. Binet has shown that after serum injections two phases occur in blood coagulability, first a stage of hypercoagulability commencing one or two hours after the injection, and lasting forty-eight hours; second. a stage of decreased coagulability occurring on the fourth or fifth day after injection and sometimes culminating in serum sickness. Increased coagulability of the blood can be induced, according to Szenes, by the application of X-rays to the spleen, and is ascribed to tissue disintegration. Tichy has found a still greater effect by irradiation of the liver. As a therapeutic measure this method might be accompanied by risk of over-dosage, and one would perhaps employ rather Nonnenbruch and Szyszka's method of splenic diathermy.

In both the conditions mentioned there is a deficiency, relative or absolute, of the primary clotting agent of the blood. This substance is derived from the tissues and blood-platelets, and is variously called thrombokinase, cytozyme, or prothrombin. Though the theories of blood coagulation differ considerably in detail, yet they have certain facts in common. The first of these is the association of thrombokinase with the phospholipins or lipoids. Bordet and Delange found that cytozyme prepared from muscle-tissue or blood-platelets had many characteristics of the lecithin group. Howell showed that prothrombin and thromboplastin reacted as lipoids, and considered that cephalin was the lipoid concerned. He found also that thromboplastin lost activity by heating to 60° C. when a protein was present, but that in the absence of protein it did not lose its power after heating to 100° C. Vines found that lecithin had no coagulative properties in the absence of ionic calcium, but that lecithin precipitated by calcium solutions was actively coagulant. Further, this calcium-lecithin compound was heat stable, but if a protein was present, activity of the solution was lost at the temperature of coagulation of the protein. Mills has concluded that a protein and a lipoid enter into the formation of tissue coagulins. There is therefore definite evidence that the agent initiating coagulation is a complex, probably an adsorption aggregate, formed of a phospholipin a protein, and calcium.

The second common factor is that coagulation will not occur in the absence of calcium salts. It is therefore possible that a haemorrhagic condition might arise, due primarily to calcium deficiency. The tendency to bleed noted in icterus has been ascribed to lack of ionic calcium, owing to its chemical combination with bile acids, but Haessler and Stebbins conclude that the bile interferes in the reaction between thrombin and fibrinogen. Even in conditions such as tetany, where, as shown by Howland and Marriott, the blood calcium falls to a very low figure, haemorrhagic symptoms are not in evidence. The injection of calcium salts by the intramuscular route will cause a temporary increase in blood coagulability; by the mouth, however, this effect was found by Addis not to occur, and Dennis and Minot find that feeding calcium salts to animals or man leads to no appreciable increase of the calcium content of the serum, except occasionally in certain animals when the initial concentration is low.

The last common factor is that thrombin reacts with fibrinogen to cause the precipitation of fibrin. It is also generally accepted that substances are normally present in the blood which antagonize the action of thrombin, and which are generically termed antithrombin. Howell's antithrombin is a substance of unknown composition, destroyed by heating to 70° C. and weakened and finally destroyed by dialysis. In Howell's theory of coagulation, antithrombin is normally neutralized by the lipoidal thromboplastin of the tissues, but Gratia has been unable to substantiate this. He maintains that the lipoids are primary coagulative agents, and that antithrombin is neutralized by the excess production of thrombin. Further, he holds that chemical union of thrombin and antithrombin does not occur, but is analogous to the union of toxin and antitoxin. Thrombin can form in the presence of antithrombin, and if fibrinogen is present, partial reaction occurs with each substance, so that the thrombin can slowly form a fibrin clot, even though neutralization of the antithrombin is incomplete. Doyon has obtained evidence suggesting that antithrombin is a nucleoprotein, as its chemical reactions are similar and also nucleinic acids possess comparable anticoagulant powers *in vitro* and *in vivo*. Minot and Denny, following Howell's theory of coagulation, studied the clotting factors in a large number of diseases, but found an increased amount of antithrombin in three cases only. Probably this factor is not of fundamental importance in haemorrhagic conditions.

The chemistry of thrombin and of its precursor thrombogen is still vague. Such evidence as exists seems to point to the association of thrombin with the globulins, as it is insoluble in alcohol and is destroyed by heating to 55° C., but the possibility must be borne in mind that, as in the case of thrombokinase, its physical characters may be due to the predominance of one constituent of a colloidal aggregate. Herzfeld and Klinger consider that thrombin is produced by intracellular protein hydrolysis, since they state that thrombogen passes out from many kinds of cell into the plasma as a higher protein-cleavage product. These authors do not consider the lipoids as essential factors in blood clotting, but rather as secondary accelerators.

The concurrence of the various theories on these points, namely, the necessity for calcium, the lipoid factor, and the action of thrombin on fibrinogen, leaves the genesis of thrombin as the subject of disagreement. Morawitz originally considered that thrombokinase reacted in the presence of calcium salts with the thrombin precursor, thrombogen, to form thrombin; this theory is in substance widely accepted at the present day. Howell considers that prothrombin was converted to thrombin by calcium salts, without the intervention of kinase. He maintains also that this reaction is continuously taking place in the circulating blood, but that intravascular clotting is prevented by antithrombin. When blood is shed, the antithrombin is neutralized by the thromboplastin derived from the tissues, and therefore the calcium-prothrombin reaction can proceed unhindered. Recently he has introduced two new substances: heparin, a phosphatide derived from the liver and previously described as antiprothrombin, activates another substance, pro-antithrombin, to form antithrombin. Heparin has also the property of preventing the interaction of calcium salts and prothrombin. The substances concerned in Howell's theory are therefoı prothrombin, calcium, thromboplastin, heparin or antiprothrombin, pro-antithrombin, antithrombin, thrombin, and fibrinogen. This theory tends to increasing complexity and perhaps decreasing probability. Bordet has found Howell's theory untenable; his own theory is in many ways similar to that of Morawitz. Lipoidal cytozyme in the presence of calcium salts reacts with a precursor to form serozyme (thrombin). This reaction is not enzymic, for it is maintained that there is a true union between these generators of thrombin, and that a given quantity of cytozyme will react only with a given quantity of serozyme. Mills and Guest would seem to go still farther, for they conclude that the lipoid and calcium in tissue coagulins unite directly with blood fibrinogen and so enter into the formation of the fibrin. This conclusion is based on the recovery of calcium and lipoid from fibrins, and it implies that normal coagulation consists of two simultaneous reactions, the one commencing with thrombokinase and ultimately forming thrombin, the other the direct union of tissue coagulin with the blood fibrinogen, since they do not consider the actions of kinase and coagulin as identical. Their experiments do not give sufficient evidence for this conclusion; the use of recalcified citrate plasma does not preclude the formation of fibrin by the more normal route, with the tissue coagulin acting as an accelerator of the reaction. Further, it is known that thrombin will precipitate fibrin from calcium-free fibrinogen solutions, and it was shown by Hammarsten some years ago that the amounts of calcium contained in fibrin and fibrinogen were almost identical.

In the foregoing pages, certain agreements of a general character in the various theories of blood coagulation are indicated, and some emphasis has been laid upon the importance of the lipoid element in the coagulation process. It may be said that the majority of the haemorrhagic states, as for instance purpura and haemophilia, and also probably the haemorrhagic diseases of the newly born, are dependent on a deficiency, either qualitative or quantitative, in the lipoid factor, and this may therefore be considered to rank of high importance in the pathology of the haemorrhagic states. The other factors in the chain of coagulative processes do not appear to play any very outstanding part in the pathology of the coagulative deficiency diseases. Calcium injected intramuscularly can in many cases cause an increase in coagulability, but deficiency of calcium rarely, if ever, is of a degree sufficient to cause deficiency of coagulation. The physiological method whereby the lipoid content of the blood is maintained normally is not yet understood, so that the methods of treating these haemorrhagic states are still, strictly speaking, empirical; the two chief methods are by the repeated injection of serum, and the induction of anaphylaxis.

Of the theories of blood coagulation recognized at the present time there is little doubt that the theory of Bordet and Delange is the most probable. It is, however, important that the fundamental principle recognized by Nolf should be remembered, though the theory he formed is not satisfactory; he was among the first to insist that blood clotting was essentially an interaction of colloidal substances. The different reactions which occur are presumably stages in the transition of an unstable colloid system in the circulating blood to a condition of stability, culminating in the precipitation of the reacting colloids in a complex of insoluble fibrin.

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H. W. C. V.

ABSTRACTS

SURGERY

Barling, G. Note on a series of 100 operations for gall-stones in private patients, with special reference to recurrence. *Brit. J. Surg.*, 1921, **9**, 221.

A case is reported of a woman of 74, who was operated upon some six or seven years previously, the gall-bladder was removed and the common duct cleared of calculi. The stones were soft and mortar-like, and therefore evidently due to an infection. At a second operation the duct was again found to be occupied by masses of soft ill-formed stone. Owing to the experience of this case the author was led to investigate the subsequent histories of his last 100 cases of operations for gall-stones. Of the 100 cases six died as a result of the operation. In the course of these 100 cases the technique had changed. In the first 50 cholecystectomy was only performed thirteen times, but in the last 50 the gall-bladder was removed in 40. He has found that the patients recover more easily and quickly after cholecystectomy and he doubts whether a drained gall-bladder ever becomes aseptic. He does not find that removal adds to the risk, but he does not remove it in cases of widespread suppuration or in very feeble patients. Thirty-five of the patients had stones in the common duct. One had a stone in the head of the pancreas, and in two it was necessary to open the duodenum for a stone impacted in the ampulla. Of the fifty-three cholecystectomies one died, and of the remaining fifty-two three have had symptoms suggesting recurrence, one of which was the case reported in the beginning of the article.

[Note by Abstractor : No note, however, is given of the number of recurrences when the gall-bladder was merely drained, nor is it stated whether in those cases of recurrence there was any evidence of an infection of the common duct. Pigment calculi are alone formed in the duct, and it would seem that sepsis is necessary for this to happen, hence, if there be pus in the duct, if it be dilated, or if the stones be soft and putty-like, recurrence is more probable.] A. J. W.

Irwin, S. T. Torsion of the gall-bladder. *Brit. J. Surg.*, 1921, **9**, 310.

The presence of a completely twisted gall-bladder is relatively rare and in only a very small proportion of such cases will torsion of the viscus occur sufficiently for it to become gangrenous. The case reported was that of a woman aged 34, who was suddenly seized with acute epigastric pain twenty-six hours before admission. There was frequent vomiting which did not relieve the pain and the bowels had acted three times. The temperature on admission was 99 and the pulse 90. No jaundice was present. The abdomen was generally rigid and there was great tenderness over the gall-bladder. At operation the gall-bladder was found to be gangrenous, tense, and black in colour. The change was due to torsion, the gall-bladder having twisted clockwise through one complete revolution. The twist was situated in the proximal part of the gall-bladder and did not include the spiral valve. Cholecystectomy was performed. (No note is made as to whether gall-stones were present.)

Several other cases are mentioned and it is stated that so far seven have been reported in the literature (but no mention is made of the case reported by Lett in 1909 and of another reported by Wendell in the *Annals of Surgery*, vol. xxix.) A. J. W.

Moore, F. D. A comparative study of the end results of cholecystostomy and cholecystectomy. *Surg. Gynec. & Obst.*, 1921, **33**, 41.

The question as to whether cholecystectomy or cholecystostomy should be the operation of choice has not yet been settled, and the author of this paper brings forward some interesting figures to throw light upon the matter. He states, in opening, that while cholecystectomy may become in the hands of experienced surgeons a relatively speedy and safe operation, yet it is undeniably true that in the hands of an occasional operator, or in the event of complications or general debility on the part of the patient, cholecystostomy must be invariably the safer operation. His paper is an attempt to compare, not the immediate relief afforded to the patient, nor the ease and safety of the operation, but the end results. Until about four or five years ago cholecystostomy was considered by most surgeons to be the operation of choice. He has studied about 3,000 cases which include his own and others reported in the literature, and there is a second report of about 250 made several years after operation.

He finds that after cholecystectomy secondary operations were required on 57 and after cholecystostomy in 89 cases. The average period of relief following cholecystectomy was two and a half years and after cholecystostomy eight to nine months. The average condition of the patient after cholecystectomy was 70 per cent. good, 20 per cent. fair, and 10 per cent. bad. After cholecystostomy 40 per cent. good, 45 per cent. fair, and 5 per cent. bad. The average mortality for both operations was 5 per cent. He states that of the various conditions found at the second operation the majority of recurrences following cholecystectomy were mechanical and largely due to errors in technique, and therefore ought to be avoided. The recurrences following drainage were largely due to the primary pathological conditions, and as such could only be prevented by a removal of the original cause. There was no evidence to show that a total extirpation resulted in any serious or permanent disorder of the body functions or metabolism, but the operation is followed by a dilatation of the ducts which occurs probably in compensation for the loss of the gall-bladder. As a result of these figures he comes to the conclusion that cholecystectomy is the operation of choice in all cases, except where general debility or serious complications make removal too dangerous or prolonged an operation. Here a cholecystostomy, followed if possible at a later date by cholecystectomy, can be done with satisfaction. A. J. W.

Burgess, A. H. **Broncho-biliary fistula.** *Brit. J. Surg.*, 1921, **9**, 221.

A case is reported at length of a woman aged 59, who had been constantly coughing up bile for five months. The trouble commenced with a sudden attack of coughing followed by the expectoration of thick white mucus. Later bile was noticed in the expectoration and had continued nearly every day since. The total amount brought up per diem was usually ten to twenty ounces, and examination revealed the presence of pure bile containing *B. coli.* No history of any abdominal trouble could be obtained. Nothing abnormal was found on physical examination or on radiography. The urine was free from bile. An operation revealed a contracted thick-walled gall-bladder which contained calculi, as did also the dilated common bile-duct. The upper surface of the left lobe of the liver was everywhere adherent to the diaphragm; so were the cardiac portions of the stomach and spleen. With difficulty the upper surface of the left lobe was freed from the diaphragm, when a rounded swelling about the size of a golf-ball and having walls of stony hardness was found adherent to the diaphragm above, to the spleen behind, and to the lesser curve of the stomach almost as high as the cardiac orifice. The calcified wall was opened with a chisel and bile and pigment masses escaped. The adhesions to the stomach, spleen, and diaphragm were divided, but it was so firmly incorporated with the liver that the extremity of the left lobe was excised with it. Sutures were placed in the cut surface of the liver and in the raw surfaces of the stomach and spleen. Owing to the depth no actual opening connecting with the lung could be found, although this was the only possible site of communication. The common bile-duct was incised and twelve calculi removed from it. From the extremity of the left hepatic duct a probe could be passed until it could be felt beneath the suture line where the portion of liver had been excised. The gall-bladder was removed and the common duct drained. Recovery was uneventful. There was a steadily diminishing expectoration of a frothy white character and quite free from bile for the first ten days. She left the infirmary soundly healed at the end of a month.

The author states that the most probable sequence of events was gall-stones in the gall-bladder and common duct, suppurative cholangitis, perforation of the left hepatic duct, formation of a small subphrenic abscess, and extension through the diaphragm into the left lung.

A description of reported cases follows, 24 having been reported by Courvoisier, 6 of which were seen during life and recovered, and 18 seen at autopsy. Of the latter 10 were due to cholelithiasis, 6 to echinococcus cysts, and 2 to ascarides. In 1897 Graham collected 11 further cases, and in 1912 Ido and Yasuda found as many as 49, including 1 of their own. The author of the present communication has only been able to find 2 cases reported since Ido and Yasuda's paper, these being reported by Roper and Stumpff. In all, therefore, there have been 52 recorded instances of broncho-biliary fistula. In all cases the primary lesion was below the diaphragm. There has not been a reported case of primary lung disease leading to such a fistula.

A. J. W.

Kidd, Frank. **Treatment of injuries of the urethra.** *Rapport du Premier Congrès de la Société Internationale d'Urologie*, Paris, 1921, 167.

In the ten years 1909–19 forty-one fresh cases of ruptured urethra were admitted to the London Hospital. Of these 41 cases 29 were caused by falling astride some object; in these there was a lacerated wound of the bulbous urethra well in front of the triangular ligament. Of the 29 cases only 1 was fatal, that of a man aged 68 with advanced renal obstruction secondary to an enlarged prostate. Of the 41 fresh cases 8 were associated with fracture of the pelvis, and of these 5 died in a few days with extensive injuries not confined to the pelvic organs and only 3 recovered. In addition to these, 2 cases were admitted which had been run over and sustained a crushing of the pelvis without fracture; in one of these the urethra was torn in the bulbous portion and in the other just in front of the bladder; both cases recovered. The remaining 2 fresh cases were injuries to the penile urethra.

The site of the rupture in the majority of cases was in the bulbous urethra, well forward of the triangular ligament, apparently from the striking object pulping the urethra against the pubic bone. Extravasation of blood beneath Collis's fascia is not always evidence that the rupture is in front of the triangular ligament, since it was seen in two of the cases of fractured pelvis where the prostatic urethra was torn off just in front of the bladder. In the 8 fresh cases of fractured pelvis the tear was in the neck of the bladder in 4, in the membranous urethra in 3, and in the bulb in one case; this last case did very well.

The treatment adopted varied. As a result of using the old-established method of suturing the ruptured urethra round a catheter and tying it in and passing bougies for a certain time afterwards, 76 per cent. of cases were practical cures and 90 per cent. had perfectly clear urine. In most of these a stricture could be found with an air distension urethroscope, but it was not of sufficient degree to be noticed by the patient.

In the case of fracture of the pelvis, although the immediate mortality was high, the end results in 5 cases years later showed that 2 were free from symptoms without dilatation, two had progressive strictures which needed regular dilatation and they suffered from recurrent attacks of cystitis; and patients who had omitted dilatation after the first year had developed a stricture which admitted an 18 F. bougie. F. J. F. B.

D'Agata, G. Sull' ematuria cosidetta essenziale. [**On so-called 'essential haematuria'.**] *Policlin.*, 1921, Sez. chir., **28**, 325.

Pizzetti, D. Contributo allo studio delle pielonefriti ematuriche unilaterali. [**Contribution to the study of unilateral pyelonephritis with haematuria.**] *Policlin.*, 1921, Sez. chir., **28**, 347.

These two papers, reporting personal cases, are published as documents illustrating the views of Professor Taddei, from whose clinic one of them emanates. They unite in ascribing both the haematuria and the alternative nephralgia to a nephritis, parenchymatous or interstitial, with only this special character, that its distribution may be not only unilateral, but of patchy distribution throughout the affected kidney. (Albarran.) Since the causation is considered as dependent on the excretion of toxins, the lesions observed are presumably areas of deficient or imperfect recovery. The pelvis of the kidney, indeed, shows an inflammatory process of proliferating papilliferous type, indicating chronicity. One of the cases reported exhibited in the pelvis areas analogous to leucoplakia of the skin and possibly ectodermal in derivation. Another case was an example of double ureter and pelvis, but this was complicated by the presence of a small calculus in one pelvis. Developmental anomalies are not uncommon in the series.

E. R. C.

Dangschat, E. Zur Ectopia testis perinealis congenita. [**Congenital ectopic perinaeal testicle.**] *Deutsche Ztschr. f. Chir.*, 1921, **165**, 351.

An account of a case of a man, aged 50, who was admitted to hospital for an inoperable rectal carcinoma. Examination showed that the right half of the scrotum was considerably smaller than the left, which was of normal dimensions and contained a testicle of normal size. The right testicle was absent from the scrotum. A swelling, the size of a hen's egg, was visible to the right of the perineal raphé between the root of the scrotum and the ischial tuberosity. The skin over this was lax, but the rugae of scrotal skin were absent; on standing the perineal swelling hung as low as the left testicle. In the swelling an oval body about the same size as the left testicle was palpable, from which a process was continued into the inguinal canal; testicular sensation was present in the body, which was therefore the right testicle. The testicle was very movable and could be pushed almost to the external abdominal ring, but returned to its position when released. A blind canal 9 mm. long was present in the glans penis immediately above the external meatus. The malformation had been present since birth and caused no inconvenience.

The patient died of the carcinoma. Post-mortem examination showed that the left inguinal region, both external and internal abdominal rings, and the external spermatic fascia on both sides were normal. On the right side a firm cord, as thick as a goose-quill, stretched from the posterior and internal aspect of the cremasteric fascia, where it covered the tunica vaginalis in a position corresponding to that of the head of the epididymus, to the perineum, fixing the testicle near its lower pole; this cord was 6 mm. long. The cavity containing the right testicle was surrounded by a firm fascia which shut it off from the scrotum. The tunica vaginalis extended to within 2 cm. of the external abdominal ring. Both testicles were of normal size and the epididymus had the normal situation with regard to the testes.

Histologically the abnormal cord consisted of connective tissue rich in elastic fibres, but without muscle-fibres. The testicular parenchyma had a similar structure on both sides. Spermatogenesis had ceased on both sides. F. J. F. B.

Frassi, L. Sieri e vaccini nella diagnosi e nella cura delle complicanze chirurgiche della blenorragia. [B] [**Serums and vaccines in the diagnosis and cure of the surgical complications of gonorrhoea.**] *Arch. ital. di chir.*, 1921, **3**, 537.

This monograph of more than a hundred pages with extensive bibliography reviews the available serums and vaccines, their methods of administration, and the results claimed for them, discussing also the theories upon which their production is based. He concludes that gonorrhoea is a constitutional disease, in which the organism finds access to the blood. Antibodies are found within a few days of infection. Diffusion is by all paths, and susceptibility is increased by all means common in other infections. There is no natural immunity, and the acquired form is transient, passing rapidly into increased susceptibility. None of the diagnostic methods dependent on immunity-reaction is reliable. Vaccines are more efficacious and safer than sera, but in articular complications the latter are worth trial. Vaccines should be polyvalent. E. R. C.

Bufalini, M. Contributo allo studio anatomico-patologico e clinico dei sarcomi della mano e alla protesi cinematica a motore alternante dell' avambraccio. [B.] **[Contribution to the clinical and pathological study of sarcomas of the hand and its kinematic prothesis with alternating motion of the forearm.]** *Arch. ital. di chir.*, 1921, **4**, 189.

The author's case was amputated through the wrist-joint. The dorsal tendons were united to the cut ends of the profunda tendons, which thus could play easily across the smooth surface of the radio-ulnar articulation. Across the front of the forearm, an inch and a half from the extremity, a transverse incision was made through the skin and superficial fascia, with a second one parallel and about half an inch higher. The adjacent edges of these two incisions were united over gauze, making a good skin-lined tunnel. The ends of the sublimis tendons were now pulled up, turned over this tunnel, and united to themselves above, through the upper incision. The profunda tendons were sutured to the bottom of the tendon-loop thus formed and the distal edges of the two parallel incisions drawn down and carefully sutured together and to the lateral edges of the tunnel. There was thus produced a skin-lined canal, which, with a few weeks' practice, the patient could pull forcibly up and down for a centimetre or two. The artificial hand, to be applied, only required suitable mechanical means of increasing the range of movement to afford a good grip and release.

E. R. C.

Wilson, L. B. Malignant tumours of the thyroid. [**B.**] *Ann. Surg.*, 1921, **74**, 129.

Diagnosis of malignant tumours of the thyroid is less frequently made in in the early stages than with any other form of malignant tumour. Treatment is therefore often delayed until it is useless, and the mortality is very high. The incidence is higher than is usually believed, as many cases are probably overlooked. The present paper is a study of the cases observed at the Mayo Clinic from January 1901 to January 1921, and completes and brings up to date the bibliography presented by Müller and Speese in 1906. In this paper there was a review of 181 cases of carcinoma and 117 cases of sarcoma. Wilson states that our knowledge of the general incidence is meagre from the lack of accurate data, and this accounts for the fact that in the published reports the incidence has varied from 1 in every 93 postmortems to 1 in every 2,546. In the Mayo Clinic the incidence was 1 in every 297.

In the papers reviewed a series of 1,430 cases showed that 991 were epithelial, 195 were sarcomas, and 244 undetermined. The cases in the Mayo Clinic consisted of 188 carcinomas, 19 sarcomas, and 83 which were not operated upon, but the author points out that in personal communications from American surgeons he has obtained details of 169 cases, whereas only 34 have been reported by American authors. In other words, only a small proportion of the cases have been reported in the literature.

The general belief that these tumours are rare is probably due to errors of diagnosis. Of a group of 97 cases occurring at the Mayo Clinic, 50 contained no suggestion of malignancy in the clinical history before the first operation, and 23 of the glands were passed by the pathologists without suspicion of malignancy. The accuracy of diagnosis has probably been greatly improved in the last three or four years. Any geographic incidence is hard to determine, and, although there was no such incidence discovered at the Mayo Clinic, it is possible that malignant tumours are more common in those districts where simple goitres abound. As regards the relationship to other forms of goitre there were at the Mayo Clinic, 10,682 simple goitres; 5,867 exophthalmic goitres, and 290 malignant tumours. None of the cases gave a previous history of exophthalmic goitre. The greater preponderance was in the fifth decade.

The sex incidence showed that 69 per cent. of the cases occurred in women. Of 290 cases, 159 had thyroid enlargement for five years or more. Only 61 had not noticed any enlargement previous to one year.

Symptoms. Usually the first symptom leading to suspicion of malignancy is a rapid increase in size. The increase is steadily progressive and not intermittent as in other thyroid enlargements. Sometimes the growth may be slow and continuous rather than a sudden and rapid increase. The surface is more apt to be irregular and nodular. Accompanying the enlargement are symptoms of pressure on the larynx, trachea, and oesophagus. Pain extending from the thyroid to the neck and behind the ears may be an early symptom. Cardio-vascular disturbances are often present, but at this stage the general health may remain good. As the disease progresses all the symptoms become aggravated. The trachea may become infiltrated and haemorrhage may develop early. Dyspnoea and dysphagia may be marked. Later the tumour becomes large, hard, and immovable. The veins of the neck and arms are distended. The skin over the tumour becomes red and adherent and the patient rapidly loses weight. Metastatic deposits are most frequent in the lungs, but the skull, brain, and liver are also frequent sites. A few cases have been reported of malignant tumours in organs distant from the thyroid in which necropsy revealed no evidence of malignancy in the thyroid gland itself.

Effects of operation. Early thorough operation gives a fair percentage of cures. While still intracapsular complete resection of the entire lobe may result in a permanent cure, but a diagnosis is seldom made at this stage. Mistakes are often made in diagnosing the condition as a foetal adenoma when it is really a carcinoma. Unless there is positive evidence of non-malignancy the operation must be radical to the extent of removing every portion of nodular adenomatous tissue at the site involved. It may even be necessary to clear out all thyroid tissue on both sides, trusting to thyroid feeding to maintain the metabolic balance. Of 207 cases operated upon at the Mayo Clinic, 194 had been heard from later. Of these, 164 had recurrences. The average post-operative life when there was a recurrence or when the condition was inoperable was six months for sarcoma and one year and five months for carcinoma.

Pathological classification. Stress is laid upon the fact that there are three types of goitre: Colloid goitre due to storage of secretion; exophthalmic goitre due to profuse proliferation of normal adult tissue; adenomas due to circumscribed proliferation. If the adenoma continues to proliferate it may penetrate its capsule and become malignant. Occasionally there is met with an adult profuse proliferation of the parenchyma without evidence of encapsulation which may be referred to simply as carcinoma of the thyroid. All other tumours associated with symptoms of malignancy are usually described as sarcomas. Besides the connective tissue elements which are usually of the spindle-celled type, there are almost invariably present large or small groups of parenchymatous cells which show they are also proliferating, and thus it is possible that they have also an epithelial origin.

A series of 135 illustrative cases follows with clear diagrams of the microscopical appearances, which are given in the hope of aiding the diagnosis. A brief account of the clinical history is given with each.

A careful study of a large series leads inevitably to the conception of the very important part played by proliferating adenomas as the starting-point of malignant tumours, the first detailed description of which was given by Langhans. Occasionally malignant tumours composed of thyroid tissue may be found growing in regions distant from the thyroid while there is a total absence of any appearance of malignancy in the thyroid itself. There was one such case in Wilson's series, the malignant tumour in this case being situated in the thorax. In other cases the epithelial cells of the metastases are not in the same stage of development as the original tumour of the thyroid. There was one such case in his series where there were extensive deposits in the lungs, pleura, liver, and abdominal lymph glands. The thyroid itself was the site of an extensive malignant tumour, most of the tissue of which was composed of cells fairly well differentiated toward the adult type. There were three or four cases with rapidly proliferating tumours which histologically were either foetal or partially differentiated adenomas which recur rapidly and extensively and yet throughout long periods show no sign of metastases.

A bibliography including 141 references follows. A. J. W.

NEUROLOGY

Roussy, G., et **Cornil, L.** A propos de deux cas de syndrome thalamique. Origine striée probable de certains troubles moteurs associés : syntonie d'automatisme, hypertonie fonctionnelle. [**Two cases of the thalamic syndrome, with motor symptoms of striatal origin.**] *Rev. Neurol.*, 1921, i, 737.

In the original account of the thalamic syndrome by Dejerine and Roussy, involuntary movements of the chorea and athetosis type were included as essential symptoms, but Roussy elsewhere expressed the view that an associated involvement of the internal capsule was the actual basis of these motor symptoms. The authors now believe that recent research on the symptomatology of lesions of the corpus striatum (*Medical Science*, 1921, **5**, 53) renders a more precise statement possible. Two cases of the thalamic syndrome with involuntary movement are described in detail and are the basis of the conclusions expressed by the authors.

The first was that of a woman of 57, who had had a 'stroke' without loss of consciousness over two years before coming under observation. The side affected was the left. When completely at rest the left limbs were flaccid, though the attitude of the arm was commonly one of flexion. When walking, and there was no appreciable weakness of the left limbs, the gait was that of a spastic hemiplegia. The arm became flexed at all joints and elevated at the shoulder, while the leg was held extended and circumducted. On forceful movements the arm showed irregular choreo-athetotic movements of alternating flexion and extension. Similarly the foot went into alternating dorsi- and plantar-flexion. In addition, the subject was quite unable to relax the muscles of the flexed arm, and indeed the effort to do so often induced an access of flexion. Voluntary movements of the upper, but not of the lower, limb were ataxic. On the sensory side the disturbances, both subjective and objective, were quite characteristic. There were formications, a sense of heaviness, and, at the time of onset, severe pain in the arm. Objectively, the acuity for touch and pinprick were unaffected. Pulling the hairs was more painful than on the normal arm, while there was painful hyperaesthesia to hot stimuli and confusion between heat and cold on the affected arm. Vibration sensation was normal on both sides. The sense of position and the appreciation of size, shape, and form were abolished in the left hand. The reflexes showed no definite qualitative alteration on the left side.

The second case was that of a woman of 61 years, who had had two strokes with loss of consciousness six and three years before coming under observation. On recovering consciousness from the second attack the patient began to experience lancinating pains in the right half of the body and to be subject to irregular involuntary movements. There was no hemiparesis on the affected right side. The flaccidity of the muscles of the affected limbs at rest, and the involuntary flexion of the arm and hemiplegic gait were as described in the previous case, the only contrast between the two being the predominance, in this instance, of choreo-athetotic movements of the affected arm. The sensory changes and the condition of the reflexes were also as described above.

In short, side by side with the characteristic sensory changes of the thalamic syndrome, there were in both cases motor phenomena of 'extrapyramidal type'. The authors maintain that disturbances of muscle-tone are the underlying basis of the involuntary changes in position of the arm and of the hemiplegic gait and attitude when walking, and also of the inability of the patient when erect to relax the arm muscles. It is doubtful, however, whether the special nomenclature they adopt to express these phenomena do not rather complicate than simplify the description. Thus, for the involuntary tonic flexion of the arm, they adopt the term 'syntonie d'automatisme', presumably in contrast to the term 'syncinésie' used by French authors to describe the involuntary associated movements of hemiplegics. The inability to relax they term 'hypertonie intentionelle', while the flaccidity at rest is called 'hypotonie du repos'. All these disorders of muscle-tone, as well as the choreiform and athetotic movements, they attribute to a lesion of the corpus striatum. In support of this thesis they refer to cases published earlier by one of the authors, in which the lesion in two cases of thalamic syndrome with involuntary movement involved the lenticular nucleus, and in two others without involuntary movement, in both of which the lenticular nucleus was practically intact.

In conclusion they suggest that there is (i) **a pure thalamic syndrome**, in which the lesion is strictly limited to the thalamus and involuntary movements are absent; (ii) **a thalamo-pyramidal syndrome**, in which the posterior part of the internal capsule is involved; and (iii) **a thalamo-striate syndrome** in which the lenticular nucleus is involved by the lesion. Although we do not yet perfectly understand the physiology of the corpus striatum, nor the origin of the involuntary movements so frequently observed in lesions of this structure, yet there is clinico-pathological evidence to justify the statement that 'choreo-athetotic movements' are associated with lesions of the corpus striatum. However, the tonic reactions described by Roussy and Cornil in the present paper cannot with any degree of plausibility be associated with striatal lesions. Phenomena indistinguishable from these accesses of tone in the affected limbs are known to occur in hemiplegia, and have been the subject of minute, but purely empirical, classification and subdivision by Marie and Foix and others. Here, as so frequently elsewhere in neurology, the true significance of various tonic muscular reactions is obscured because neurologists have not so far adopted the physiological conception of muscle-tone as a postural reflex. Accompanying every voluntary movement is a tonic reaction, or a postural adaptation, directly proportional in complexity to the movement it accompanies. These modifications of tone are as much a part of a perfectly co-ordinated movement as the actual progress of the limb through space. When, as in cerebellar lesions, they are abolished, the grossest disorders of co-ordination result. What Jackson called the 'complementary inverse' or 'corresponding opposite' of this ataxy from loss of postural tone, would be a condition in which, while voluntary movement was abolished from a pyramidal lesion, the tonic postural reactions which normally occur on the reflex level persisted. In these circumstances they would be expected to appear in an exaggerated form owing to their 'release' from higher control. Now postural reactions are necessarily bilateral. Therefore, in a hemiplegia, we should expect to see on the paralysed side uncontrolled tonic postural reactions, or alterations of tone, during all movements of the normal side, which were sufficiently widespread or forceful to demand postural adaptation of the opposite half of the body. In other words, as has been suggested elsewhere (*Brain*, 1919, **42**, 1), the appearance of what are called associated movements of the paralysed limbs in hemiplegia is a phenomenon to be anticipated. The associated movements which do actually occur are, to judge by their characters, not so much movements as accesses of tone in the limbs, and therefore the conclusion seems justified that they are simply uncontrolled postural or tonic reactions.

From what is known of the maintenance and regulation of tone, from the researches of Sherrington and Magnus, there is no evidence that the corpus striatum plays any part in the processes in question.

Therefore, Roussy and Cornil's conclusion in this respect must be regarded as devoid of foundation. There is an ever-increasing tendency to make the corpus striatum responsible for all inexplicable forms of involuntary motor activity. It is, in consequence, all the more desirable that it should not be made a dumping-ground for motor reactions which are capable of another and less speculative interpretation.

F. M. R. W.

Kato, G., Shizume, S., and **Maki, R. The nature of the paralysis of nerve in the birds with beriberi-like disease.** *Japan Med. World*, 1921, **1**, 43.

The authors preface their observations with the remark that no adequate study of the true nature of the paralysis in polyneuritis avium has yet been made. They investigated the rate of conduction of the nervous impulse in healthy fowls and found it to vary between 68 and 57 metres per second, the average rate being 63 metres. The reaction-time of fowls' muscle was then found to be 0·0085 second, the duration of the muscle twitch obtained by direct stimulation of the motor nerve 0·09 second, and the maximum height of the twitch 45 to 53 millimetres. Having established these standards by the examination of eighty birds, they then proceeded to determine what alterations resulted from an exclusive diet of polished rice. They found that the velocity of conduction of the impulse was constantly reduced, generally by at least 50 per cent. To obviate the complicating influence of the lowered body-temperature of birds suffering from avian polyneuritis, the preparations were examined in a moist chamber at a constant temperature. Whereas, in normal birds, the maximum twitch of the muscle is constant no matter at what point on its course the nerve is stimulated, in diseased birds the twitch varied in height according to the distance of nerve to be traversed by the impulse; the greater this is, the smaller the contraction. Similarly, the reaction-time and the duration of the twitch were also prolonged. A comparative investigation of birds suffering from inanition showed that the conduction-rate was normal.

The authors conclude that conductivity is impaired in polyneuritis, but not in inanition.

In a further series of investigations it was found that all these disturbances of nerve function could be reproduced by the action of hydrogen ions on the nerve. They state that birds suffering from avian polyneuritis can be cured so rapidly that one cannot correlate the paralysis with histologically discoverable lesions in the nerves, 'but if we consider the paralytic state is due to the action of some toxic substance such as hydrogen ions on the nerve, and the recovery is effected by removing them with injection of rice bran extract, the entire phenomenon is easily conceivable.' They found that within a few hours of injection of rice-bran extract into paralysed fowls, the conduction-rate was restored to normal. If a nerve were experimentally paralysed by submersion in an acidified Ringer's solution, it recovered much more rapidly when the acid solution was replaced by Ringer containing rice-bran extract than when it was replaced by ordinary Ringer. On the other hand, rice-bran extract had no curative effect upon the paralysis induced by chloral hydrate, cocaine, or urethane. Paralysed nerves and also the blood of paralysed fowls in avian polyneuritis were found to contain excess of hydrogen ions. Starved fowls were normal in both respects. Paralysed nerves adsorbed hydrogen ions more readily than normal nerves, while finally, nerves paralysed by hydrogen ions directly applied showed changes comparable with those found in polyneuritis. The authors therefore regard the adsorption of hydrogen ions as the direct cause of the paralysis in avian polyneuritis.

From the neurologist's point of view perhaps the chief interest of these observations is that they indicate that the conductivity of nerves in this condition is impaired. This bears out the views recently expressed in a review in this journal (1922, **5**, 314) that attempts to correlate histologically observed degeneration with paralysis are futile under these circumstances, but that in spite of this the paralysis is in all probability the result of impaired conductivity of nerve fibres rather than that of obscure histological alterations of the cell body. F. M. R. W.

KRABBE, K. H. Les hypertrophies musculaires postnévritiques. [**Postneuritic muscular hypertrophy.**] *Rev. Neurol.*, 1921, ii, 802.

Krabbe describes a case of localized muscular hypertrophy in an otherwise healthy young fisherman of 21. The muscles involved were those of the calf, and the condition was of eight years' standing, having developed after a sudden paralysis of both legs, associated with pain. Recovery had been gradual but never complete, and at the time of examination he complained of ready fatigue and of aching pain in the affected muscles. The circumference of each calf was 18 inches. The muscles were normal in consistence, both when at rest and in contraction. The power developed was less than normal. The electrical reactions showed no qualitative change, but were less facile than normal. There were no other signs of nervous lesion.

The patient submitted to having a small piece of the right calf muscle removed for examination. Microscopically, it was found that the fibres were very variable in diameter, being for the most part enlarged, but abnormally small fibres were also seen. There was no sign of inflammatory reaction, and no increase of connective tissue. There were numerous nuclei scattered throughout the substance of the fibres.

Krabbe has collected and summarized accounts of about twenty similar cases from the literature. In the majority, the onset followed an acute infection, typhoid being the disease most frequently responsible. Commonly, the onset is accompanied by weakness, pain, and often by sensory loss of a distribution corresponding to the topography of the affected musculature. Power is generally somewhat below normal, and unduly ready fatigue and pain are recorded as common symptoms. The electrical reactions are commonly diminished or lost without qualitative change.

In such cases as were microscopically examined, the usual finding was hypertrophy of the muscle fibres without sign of inflammatory reaction or increase of connective tissue. Léri has classified muscular hypertrophy into (1) functional hypertrophy, (2) hypertrophy preceding the onset of atrophy, (3) hypertrophy in Thomsen's disease, and (4) hyperplastic muscular dystrophy. Krabbe considers all these cases to belong to the last-named group, which, however, includes cases of varying origin. Probably a localized neuritis is the exciting cause. In this connexion a case reported by Lhermitte is of interest. The patient was a soldier wounded in the buttock in 1915. The sciatic nerve was injured and there was paralysis of the muscles below the knee. Accompanying this was a hypertrophy of the muscles of the calf and of the hamstrings. The affected muscles were firm and of the consistence of india-rubber. They did not respond to faradism.

Krabbe quotes Léri's article in Pierre Marie's *Pratique Neurologique* as containing the best general account of the condition.

F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Gengou. Les substances bactériolytiques des leucocytes et leurs rapports avec l'alexine. [**The bacteriolytic substances of the leucocytes and their relation to alexine.**] *Ann. de l'Inst. Pasteur*, 1921, **35**, 497.

For many years there has been a steadily growing literature on the question of the relation existing between bactericidal substances which can be extracted from leucocytes and the complement (alexine) of serum. The main conclusions reached were clearly summarized by Levaditi in the *Bull. de l'Inst. Pasteur*, 1914, **12**, 481, 529, 577. The present author has made a further study of the problem. His method was to produce a peritoneal exudate in rabbits by injection of bouillon. The cells, being collected, were repeatedly washed in Ringer's solution and diluted down so that 1 c.mm. contained 40,000 leucocytes. The deposit of leucocytes was then treated with 2 to 5 vols. of a centinormal HCl, the mixture being kept for an hour at least at 6–8° C. After centrifugalization the acid was exactly neutralized by centinormal soda, which induces the formation of a precipitate. This is removed by the centrifuge, the supernatant liquor constituting the leucocytic extract. With such an extract spherulation was caused in cultures of cholera, typhoid, and other bacteria exactly like that which is seen with immune serum. As the author points out, spherulation therefore cannot be definitely ascribed to the action of complement. The spherulation is also not due to the action of proteolytic ferments in the cells. W. B.

Caruso. Sulla conservazione del complemento. [**On the preservation of complement.**] *Pathologica*, 1921, **13**, 184.

Complement can be preserved for a relatively long time if kept frozen at a temperature of $-10°$ or $-15°$ C. As, however, only a few laboratories possess a suitable freezing apparatus, Austin (*J. Am. M. Ass.*, 1914, **62**, 868) and Thompson (*ibid.*, 1916, **66**, 652) had recommended diluting the guinea-pig serum with a hypertonic salt solution. Their method was not found satisfactory by Rhamy (*ibid.*, 1917, **67**, 973), who proposed diluting the serum with a 10 per cent. solution of sodium acetate. The usefulness of this process was quite recently confirmed by Dold (*Deutsche med. Wchnschr.*, 1920, **46**, 1, 62), and Hammer-Schmidt (*München. med. Wchnschr.*, 1920, **67**, 1382). Caruso has made further experiments with Rhamy's method and found that it gives good results if the serum be obtained under strictly aseptic conditions. To ensure this a small quantity of powdered chloretone may be added to the sodium acetate solution, by which means the complement, even if not sterile, keeps well for at least five days. C. d. F.

Izar, G. Sul metodo di Kaup per le prova della fissazione del complemento nella sifilide. [**On Kaup's method for the complement-fixation test.**] *Haematologica*, 1920, **1**, 508.

Rapisardi, S. Sulla proprieta fissatrice specificà del siero nella reazione di Wassermann-Kaup modificata. [**On the specific fixing property of the serum in the Wassermann-Kaup test.**] *Pathologica*, 1921, **13**, 65.

Among the various modifications of the complement-fixation test that of Kaup (1917) deserves particular mention because of its greater delicacy in comparison to the original method of Wassermann. Kaup establishes the 'complement unit' by titrating the guinea-pig serum for the mixture of antigen and human normal serum, with the object of eliminating causes of mistake due to the anticomplementary properties either of the serum or of the antigen. Izar points out that this presupposes a theoretical possibility which has no practical existence, since we do not possess a standard normal serum the anticomplementary power of which could be used to establish the anticomplementary properties of sera in general. The differences due to vegetative life are often so great that no general inferences can be made from the results obtained by the titration of one serum or even various particular sera. To obviate this difficulty, Izar proposes to add to the series of serum plus antigen plus increasing doses of complement a parallel series without antigen. From a comparison between the two he deduces the limit of the anticomplementary non-specific property of a given serum, and consequently the specific complement-fixation power. In this case, and if the reaction is carried out immediately afterwards, the two control tests, normal serum and haemolytic system alone, become useless, and can be left out. But if the sera under examination are 2 or 3 days old, they acquire very marked anticomplementary non-specific properties capable of fixing even five 'complement units' in a series without antigen. In such an instance the two series, with and without antigen, might give the same results and thus render unreliable and even worthless the results obtainable by the final reaction. To obviate this Rapisardi proposes to eliminate these non-specific anticomplementary substances by precipitating the globulins by Sach's method (*Berl. klin. Wchnschr.*, 1908, **45**, 494, 699; *Deutsche. med. Wchnschr.*, 1908, **34**, 2151), and using, for the definite test, the precipitate washed with distilled water and re-dissolved in physiological salt solution. By working under such conditions he has reached the following two conclusions: (1) After the elimination of the non-specific anticomplementary substances the modified W.-K. test can be carried out with quantities of serum greater than the usual amount of 0·1 c.cm., the final results being in no way altered by non-specific complement fixations. (2) The modified W.-K. test, in allowing one to use relatively large quantities of sera having a very weak complement-fixation power, renders it possible to obtain positive results even in cases apparently negative by the ordinary method. C. d. F.

Eisler, M., u. **Silberstein, F.** Beiträge zur Bakterienagglutination. [**Studies on bacterial agglutination.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **93**, 266.

This is a long and complicated paper dealing with the agglutinating vagaries of typhoid bacilli according as they are grown on moist agar or on agar that has been kept till it is very dry. Grown on the latter, typhoid bacilli are much less agglutinable than on moist cultures, a result which the authors correlate with the greater amount of nucleo-protein when the bacilli are grown in the moist state. The agglutinogens of the two different cultures of typhoid are not identical. Those grown on dry agar are much less easily brought down when suspended in an emulsion, but this takes place entirely in the second phase of agglutination, as in the adsorption phase the two cultures are comparable. The inhibition of sedimentation is attributed by the authors to a nuclein-like body. W. B.

Burnett, T. C., and **Schmidt, C. L. A.** **Immunological experiments with catalase.** *J. Immunol.*, 1921, **6**, 255.

Experiments in rabbits to determine whether catalase is antigenic. The catalase was prepared from calf or ox liver by mincing the latter and extracting with water, the extract being then poured slowly into acetone, which brings about precipitation. After filtration the residue was evaporated, and extracted with water, being subsequently precipitated with acetone and dried again. Although grossly contaminated with tissue proteins, the preparation was very active in liberating oxygen from neutral peroxide of hydrogen. Rabbits were injected with the catalase preparation, and their sera tested alongside normal sera for catalytic and anticatalytic powers. Although a precipitin was produced by the inoculation of the impure catalase and carried with it the catalase in the presence of antigen, there was no evidence of the production of a true anticatalase.

W. B.

Schmidt, C. L. A. Immunological experiments with denatured and insoluble proteins. *J. Immunol.*, 1921, **6**, 281.

The author has studied the antigenic properties of denatured and insoluble proteins when injected into rabbits. The complement-fixation antibodies were those tested. The following antigens were employed: (1) egg albumin heated to 110° C. for 1 hour; (2) native (unheated) egg albumin, reaction P_H 7·2; (3) native (unheated) egg albumin, reaction not adjusted; (4) egg-albumin solution heated to 100° C. for 15 minutes, initial reaction P_H 7·2. All the sera of the immunized animals gave like results, indicating the presence of fixation antibodies, and there was no evidence of specificity with respect to the antigen employed. The immune sera reacted with the egg albumin irrespective of whether the latter was native or denatured, provided its solubility was not lost. In addition, two rabbits were immunized with casein, their sera being subsequently examined with sodium caseinate as the antigen. In both cases the results were positive.

W. B.

Maltaner, F., and Johnston, Elizabeth. Observations on the agglutinative and hemolytic action of calf serum on sheep cells. *J. Immunol.*, 1921, **6**, 271.

It is well known that normal bovine serum is capable of agglutinating many different kinds of red blood corpuscles. The authors have studied the phenomenon of the agglutination of sheeps' corpuscles by calf serum, and have come to the conclusion that it is caused by the formation of fibrin induced by the reaction of the cytozyme present in the suspension of sheeps' corpuscles and the other elements necessary for clot-formation which are present in the calf serum. The fibrin forms around groups of cells as centres of coagulation and precipitates out, carrying down the suspended red cells.

W. B.

Trommsdorff, R. Zur Frage der Steigerung des Agglutinintiters durch grosse Blutentziehungen. [**The increase in agglutination titre after large venesections.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **32**, 379.

In 1917, Hahn and Langer stated that in rabbits an enormous increase in the agglutinative titre of the serum ensued upon daily removals of considerable quantities of blood. Landau (1918) and Klinger (1918) failed, however, to confirm this. Most of the experiments were carried out with easily agglutinated bacteria like *B. typhosus*, *B. paratyphosus*, and *V. cholerae*. The present author reports two experiments made with *B. diphtheriae*, an organism hitherto deemed very unsatisfactory from an agglutinogenic point of view. Two rabbits received four separate doses intravenously of a culture of diphtheria bacilli killed at 56° C. Ten days after the last injection, and after the withdrawal of 20 c.cm. of serum, the latter showed a titre of 1:160 (320) which, on the following day after the removal of a further 15 c.cm. of blood, was 1:2,500 (5,000), although it was not driven higher by succeeding venesections. In the second rabbit a maximum of 1:640 (1,250) was reached, and actually a titre of 1:160 was obtained a day after the serum had shown no agglutination at all. W. B.

Lange, A. Zur Frage der Hitzebeständigkeit der gebundenen Antikörper. [**On the resistance to heat of antibodies which have been fixed.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **32**, 449.

Experiments on a number of strains of *B. typhosus* and *Proteus* X 19, to see whether the exposure of bacteria to a temperature of 100° C. influences their capability to combine with agglutinin, and whether, when such a union has taken place, it can be ruptured at a similar temperature. The author found that heated (100° C.) cultures combined quantitatively with agglutinins like the normal (unheated). The union having taken place is very heat-resisting, a result in opposition to that obtained by Bessau (1911) and Spät (1921). W. B.

Tsukahara, I. Verlauf der Agglutininbildung bei Infektion normaler und immunisierter Tiere. [B.] [**The course of the agglutinin formation in normal and immunized animals.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **32**, 410.

This paper deals with the course of agglutinin curves obtained in immunized rabbits subsequently injected with the homologous or with heterologous bacteria. The time between the first and second series of inoculations was four to six months, the cultures employed being *B. typhosus*, *B. dysenteriae* (Flexner-Y), *V. cholerae*, and *B. paratyphosus* in different combinations. After a single injection of one of these bacteria the agglutinins appear on the third day, reach a maximum in six to eight days, and begin to disappear in fourteen days, although traces can be found for many months in the serum. If, now, when the agglutinins are at a low ebb the same dose of the same culture is again injected, the author finds that the incubation period is unchanged, and there is no quickened reaction in the re-formation agglutinins. If, under similar circumstances, a heterologous antigen is employed for the second immunization process, agglutinins are formed for the heterologous antigen as in a normal animal, and also, although not regularly, for the first antigen. This non-specific reaction is called the ‘anamnestische Reaktion’ (i. e. the reaction indicating the ‘history’ of the case). The ‘anamnestische Reaktion’ shows, as a rule, an incubation period of some days, the titre of the serum increases, and then falls by degrees, as in the case of the curve of the secondary (i. e. heterologous) agglutinating curve. It is rare for a latent period to occur in the re-development of the original agglutinins following the introduction of the second antigen. The author, as a result of his experiments, finds no grounds for the belief that, after the disappearance from the serum of antibodies, the organism reacts to a new stimulus with increased rapidity of antibody formation. At the most there is merely an increase in the antibody content. W. B.

Aoki, K. Studien über die Beziehungen zwischen der Haupt- und Mitagglutination. [**Studies on the relations between agglutination and co-agglutination.**] *Tohoku J. Exper. M.*, 1921, **2**, 142.

This paper deals with agglutination experiments carried out on 18 strains of *B. paratyphosus* B, 9 of *B. typhi murium*, 3 paratyphoid-like bacteria isolated from guinea-pigs, 1 strain of *B. psittacosis* and 1 of *B. aertrycke.* According to the author's experiences cross-agglutination differentiates these bacteria into two groups: (1) including those which cause typhoid-like disease in man, and (2) those which are associated with meat poisoning or with disease in animals. The second group agglutinogenically falls into two sub-groups, viz. (1) that represented by *B. typhi murium. B. psittacosis,* and races from guinea-pigs, and (2) *B. aertrycke* and one race of *B. typhi murium.* Strains of the first sub-group of Group II are allied so closely to bacteria of Group I agglutinogenically that they can scarcely be differentiated. W. B.

Aoki, K. Über die agglutinatorische Einteilung von Dysenteriebazillen. [**On the agglutinogenic differentiation of dysentery bacilli.**] *Tohoku J. Exper. M.*, 1921, **2**, 142.

The author has made a study of the agglutinogenic properties of 4 strains of dysentery bacilli of the Shiga-Kruse type, and of 39 strains of so-called paradysentery bacilli. His results lead him to the belief that it is possible to differentiate no less than eight groups by the tests employed.

W. B.

Haendel, L., u. **Joetten, K. W.** Ueber chemotherapeutische Versuche mit '205 Bayer', einem neuen trypanoziden Mittel von besonderer Wirkung. [**Chemotherapeutic experiments with '205 Bayer', a new trypanocidal remedy of unusual action.**] *Berl. klin. Wchnschr.*, 1920, **57**, 821.

Mühlens, P., u. **Menk, W.** Ueber Behandlung von menschlicher Trypanosomiasis mit 'Bayer 205'. [**The treatment of human trypanosomiasis by 'Bayer 205'.**] *Münchcn. med. Wchnschr.*, 1921, **68**, 1488.

If the authors' claims are substantiated, 'Bayer 205' must be regarded as the most remarkable chemotherapeutic substance yet investigated. No hint is given as to its composition or mode of preparation on account, as it is stated, of the unprotected conditions of German industries in foreign countries. The preparation made by the firm Friedr. Bayer & Co. in Elberfeld is a white powder easily dissolved in saline solution or distilled water, neutral in reaction, without smell and with a slightly bitter taste. It is stable and can be sterilized without deterioration or change. It possesses extraordinary parasitotropic action on trypanosomes, and in minute doses can produce a 'sterilisatio magna' in animals heavily infected with these parasites. The toxic dose for mice is 0·018 to 0·02 gm. while cure has been obtained with 0·0005 gm. ($\frac{1}{2}$ mgm.), the relation of the curative to the toxic dose being 1 : 40 (or more). In one case a mouse heavily infected with Nagana was permanently deprived of its trypanosomes with a dose of 0·00003 gm. of 'Bayer 205'. Similar results were obtained in mice infected with dourine trypanosomes and with *T. congolense.* Rats, guinea-pigs, rabbits, dogs, and an ass were also cured of trypanosome infections. Remarkable to relate is the fact that mice simultaneously inoculated with trypanosomes and a dose of 0·001 gm. 'Bayer 205' not only remained free from infection, but could not be reinfected even 14 days later. After 24 days from the date of injection of the drug a certain percentage of mice were successfully reinoculated. The trypanocidal effect of the drug was demonstrated not only *in vivo* but also *in vitro*, the parasites exhibiting degenerative changes and finally disappearing from view. Trypansomes left in contact with solutions of 'Bayer 205' for 1½ hours were no longer infective. It is remarkable that the drug was found inert upon infections with *T. lewisi* and *T. cruzi.* It is briefly stated that the drug has also been found effective on *T. gambiense*, but this will be the subject of another communication.

Although dealing with treatment the communication of Mühlens and Menk will arouse great interest among students of protistology and chemotherapy, as their results confirm the experimental results of Haendel and Joetten. Two human cases have been treated, the one with an unsatisfactory result, the other—a severe one—apparently with a cure. The first case, a man from Fernando Po, was infected with *T. gambiense* in October 1919, and suffered from multiple enlarged lymph glands, fever, and erythema. His blood revealed the presence of trypanosomes. He received 0·25 gm. of 'Bayer 205' intravenously, followed by a similar dose seven days later, the result of which was apparently stimulating rather than destructive to the trypanosomes. He then received 11 injections of tartar emetic (total quantity 1·06 gm.) which apparently cleared the blood of parasites up to the time when the patient voluntarily discharged himself from the hospital. A later report indicated that he was not cured.

The second case, an Englishman, became infected with *T. rhodesiense* and was treated in Rhodesia without effect. Between October and December 1920 he received 3·28 gm. of tartar emetic, 0·1 gm. antimony oxide, and 2·47 gm. of soamin without being cured, although for a period of 12 days trypanosomes could not be found in his blood. On their reappearance he was subjected to 13 injections of stibenylin (total 3·05 gm.), but three days after the last and maximal dose of this drug, trypanosomes were again found in his blood, and fever ensued. A return was therefore made to tartar emetic treatment, but without benefit. He now returned to England and was treated in the Liverpool School of Tropical Medicine with many remedies, including tartar emetic, of which he received intravenously a total of 22·7 gm. during 8½ months. The result was not encouraging, and the patient arrived for treatment in Hamburg (July 3, 1921) in a miserable condition, emaciated, depressed, and anaemic. There was a definite enlargement of the spleen, and on July 9 individual trypanosomes were found in his blood. On this day he received 0·5 gm. of 'Bayer 205' intravenously, and after a two days' pause 1·0 gm.; three days later another 1·0 gm., and with similar pauses injections of 1·0 gm. till he had received a total of 6 gm. Within 16 hours of the first inoculation, trypanosomes had disappeared from his blood (two examinations daily and animal inoculations) and he rapidly recovered. Up to August 29 parasites were not found in his blood. The latest report, September 13, indicated that the patient was perfectly well and had increased over a stone in weight. After one of the injections some albumin and a few red and white blood corpuscles appeared in his urine, but otherwise no untoward symptoms were observed as the result of the treatment.

W. B.

Glenny, A. T., and Südmessen, H. J. Notes on the production of immunity to diphtheria toxin. *J. Hyg.*, 1921, **20**, 176.

Under this somewhat deprecatory title the authors give an elaborate account of the present state of researches upon which they have been engaged for a number of years. They disclaim any special novelty of result, but opine that their work gives 'a clear and quantitative value to an idea that is foreshadowed in several places in the literature of immunity'. If we follow them correctly, this 'idea' refers to the difference in response of two individuals to infection or inoculation, depending upon their different state of susceptibility or preparation, an idea crystallized in v. Pirquet's 'Allergie', leading to a 'beschleunigte Reaktion' after previous sensitization.

The authors' investigations will clearly supply a stimulus (and further experimental foundation, which is now largely lacking) for the practice of preventive immunization against certain diseases, notably diphtheria. It will be recalled that just before the war v. Behring applied the principle of preventive immunization against diphtheria with toxin-antitoxin mixtures to man, making use of a more or less secret remedy which he named 'T.A.'. Since then Park and his collaborators in America have worked out and elaborated the method on a very large scale, with results which need not be discussed in detail. In general it has been found that whereas it is easy to immunize children who are already to some extent immune by reason of 'normal' antitoxins in the blood, the non-immune children are much less easily affected by the process. The reason for this phenomenon, perhaps already guessed at, is made clear by the present authors. They show an essential difference in the response to the 'primary' and 'secondary' stimulus. If a person with no antitoxin, that is, a person who has never been infected by the diphtheria bacillus ('cryptically', 'larvally', or otherwise) is injected with diphtheria toxin, a latent period is observed during which no immunity response takes place, lasting on the average three weeks, and it is not until eight weeks have elapsed that definite antitoxins appear in the blood. This they term the 'primary response'. On the other hand, if the same treatment is applied to a person already slightly immune (with normal antitoxins), whether the immunity is derived from previous 'larval' infection or from previous inoculation, the 'secondary response' is much more rapid (incubation period on the average four days) and a high degree of immunity is quickly attained.

These observations should facilitate the immunization of non-immune children with toxin-antitoxin, or even, perhaps, with toxin alone, since they suggest the importance of a proper spacing of doses. They also, as the authors point out, support the theory, which is not generally accepted, that the normal immunity to diphtheria is dependent upon previous infection, since the secondary stimulus is the same whether the initial immunity is 'normal' or due to inoculation. P. F.

Tongs, M. S. The effect of the diphtheria toxin on the blood and hemopoietic organs of rabbits. *J. Infect. Dis.*, 1921, **29**, 408.

The author's work on the action of haemolytic streptococci on the haemopoietic organs has already been referred to (*Medical Science*, 1922, **5**, 339). In the present communication he deals with the effect of intravenous injections of diphtheria toxin on the blood corpuscles and blood-forming organs of rabbits, and he shows in tabular form that a massive dose of the poison usually leads to leucopenia which prevails throughout the course of the intoxication. In stained films the leucocytes were found to exhibit marked degenerative features, and after death the marrow showed no evidence of hyperplasia. He regards the leucopenia as a direct deleterious effect of the toxin rather than the result of unequal distribution in the blood-vessels and viscera. In animals which received diphtheria antitoxin prior to the toxin there was no appreciable leucopenia. In experiments made *in vitro* it was found that diphtheria toxin exerts a direct prejudicial effect on leucocytes—an action which can be neutralized by antitoxin. Histological changes in the marrow, spleen, and lymph nodes, are also considered in some detail. W. B.

Müller, E. F. Ueber die Bedeutung des blutbildenden Markes der Röhrenknochen für den Ablauf der akuten Infektionskrankheiten, mit besonderer Berücksichtigung der Grippe. [**The importance of the red marrow of the long bones for the course of acute infections, especially influenza.**] *Ztschr. f. Hyg. u. Infectionskrankh.*, 1921, **93**, 223.

The author has carried out a series of investigations of the bacterial content of the red marrow of the vertebrae in a large number of cases of influenza, pneumococcic, streptococcic, and other infections, and has shown by cultivation that it is infected in a very high percentage of cases. In virtue of this infection he believes that its leucopoietic function is reduced and a new development of active germ-free marrow now occurs in the long bones and is associated with a leucocytosis. The infection of the marrow of the long bones in certain diseases, e. g. enteric fever, is associated with leucopenia and confirms the author's opinion of the importance of the marrow of the long bones as a defence against infection. He applies these statements to the case of epidemic influenza, and concludes that, as the marrow of the long bones is mostly free from cultivable bacteria, and as there is at the same time a leucopenia, the virus of the disease is one that has not yet been cultivated and is presumably not *B. influenzae*. W. B.

Pentimalli, F. (1). Studi sull' intossicazione proteica. I. Introduzione. [**On protein intoxication. I. Introduction.**] *Riforma med.*, 1921, **37**, 532.

Pentimalli, F. (2). II. Tossicità dell' albumina di uovo e suoi derivati [**II. Toxicity of egg-albumin and its derivatives.**] *Gazz. internaz. di med.-chir. ed igiene*, 1921, **29**, 65.

Pentimalli, F. (3). III. Tossicità del peptone. [**III. Toxicity of peptone.**] *Rassegna internaz. di clin. e ter.*, 1921, **2**, 185.

Pentimalli, F. (4). IV. Tossicità del latte e suoi derivati. [**IV. Toxicity of milk and its derivatives.**] *Pediatria*, 1921, **29**, 481.

Pentimalli, F. (5). V. Comportamento della pressione del sangue e della respirazione. [**Behaviour of blood-pressure and respiration.**] *Folia medica*, 1921, **7**, 321.

Pentimalli, F. (6). VI. Comportamento della temperatura del corpo. [**VI. Behaviour of the body temperature.**] *Arch. d. sc. biol.*, 1921, **2**, 44.

Pentimalli, F. (7). VII. Il nistagmo. [**VII. Nystagmus.**] *Riforma med.*, 1921, **27**, 578.

Pentimalli, F. (8). VIII. Alterazioni morfologiche del sangue. [**VIII. Morphological alteration of the blood.**] *Haematologica*, 1921, **2**, 527.

Investigations on protein intoxication have up to the present been made with the purpose of either studying its immediate consequences (acute poisoning) or of elucidating the phenomena of anaphylaxis. Pentimalli has undertaken the experimental study of protein intoxications, slight or severe in character, but in any case protracted as long as possible (chronic poisoning). Various sets of experiments were therefore made with the object of testing the toxicity of egg albumin and yolk, of peptone, and of milk and its derivatives when injected intravenously into rabbits. The results obtained are: (1) The primary toxicity of egg albumin and of yolk is very small. The toxicity of the products of their hydrolysis varies according to their composition. The most toxic are the protamins, rich in diamino acids (salmine, sturine, &c.), while the monoamino acids have almost no effect. Repeated injections of protein substances of the egg-albumin type, whether primarily toxic or not, all end by being fatal to the animals, which die with symptoms of anaphylactic shock. (2) The degree of toxicity of peptone changes according to the individual sensitiveness. But in favourable conditions it is possible, by means of Rosenau and Anderson's method, to prolong the treatment for a considerable time. The animals acquire no immunity against increasing doses, but become insensible to equal doses. During the treatment anaphylactic phenomena are sometimes observed. By means of repeated injections of meat peptone it is possible to cause in rabbits a state of general cachexia ending fatally even if the treatment is stopped. (3) The primary toxicity of milk and its derivatives is approximately the same as that of egg albumin. But it is possible to prolong the treatment in such a way as to cause a cachectic state similar to that obtainable by means of peptone.

Having thus tested the toxicity of the protein substances considered, Pentimalli proceeded to investigate the behaviour of the blood-pressure and respiration, the variations in the body temperature, nystagmus, and the alterations of blood corpuscles in the intoxicated animals. The blood-pressure is not influenced by caseine and pure egg albumin. The product of hydrolysis of the latter, milk, and peptone lower the blood-pressure with consequent troubles of the respiration. The body temperature shows a temporary increase after a first injection of egg albumin, milk, and peptone. The effect of subsequent injections changes a little according to the protein used and to an undetermined individual factor. However, if the same protein is used and injections are repeated at regular intervals of 24 hours, the body temperature shows, toward the 4th or 5th day, a diminution which may have a permanent character. In this case the animals die with anaphylactic symptoms even if the treatment is suspended. This fatal termination may be avoided if the doses of the subsequent injections are smaller than that of the first one. If, after having suspended the treatment for a few months, another injection of the protein used originally is made into the same animal, the body temperature again shows an increase. This shows that an immunization of the thermogenetic centres does not take place, though a certain degree of general immunity must be present since the animals become accustomed to progressively diminishing doses, and since Bordet, Gengou, and Moreschi have shown that this is due to the formation of true antigens. Nystagmus may appear together with other anaphylactic symptoms, or be the only manifestation of a protein intoxication.

It may or may not be accompanied by pendular oscillations of the head and dilatation of the iris. It is reduced and abolished by the action of ether. As a rule it quickly disappears, but in a few cases Pentimalli saw it lasting for some hours. The morphological alterations of the blood vary a little according to the nature of the protein injected, and to the length of the treatment. A first injection of 5 or 10 c.cm. of egg albumin or of the product of its hydrolysis causes a slight leucopenia. The prolonged treatment with the same preparation causes a remarkable diminution in the number, aspect, and staining properties of red blood corpuscles. There is, at the same time, a leucocytosis which is generally lymphocytic and monocytic in character but sometimes pseudo-eosinophil. In both cases unripe cells of the granulocytic series make their appearance. These changes are generally followed by a noticeable increase in the number of platelets. When yolk is used these changes are more intense and characterized, in the end, by a polynucleosis and by the presence of dividing leucocytes. Meat peptone causes alterations similar to those due to egg albumin. The effect of milk is like that of yolk. But the lymphocytic and monocytic leucocytosis has, in the case of milk, a very lasting character, and was observed even five months after the suspension of the treatment. If the milk is boiled such effects are not obtained. As to the mechanism of production of these changes, Pentimalli is of the opinion that egg albumin and its derivatives cause at first an anaemia to which the changes visible in the circulating blood are essentially due, while yolk and milk appear to act primarily as stimulants of the haematopoietic organs. C. d. F.

Bezssonoff, N. Sur une réaction colorée commune aux extraits antiscorbutiques et à l'hydroquinone. [**On a colour reaction common to antiscorbutic extracts and to hydrokinone.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 466.

By modifying Folin's phenol reagent the author has succeeded in evolving a colour reaction for vitamin C. B.'s formula is:

Sodium tungstate	100 gm.
Phosphomolybdic acid	20 gm.
Concentrated phosphoric acid	17 c.c.
Aq. ad	1,000 c.c.

Then add to the above an equal quantity of normal H_2SO_4 and do not boil.

Unlike Folin's reagent this one will not give a reaction with a variety of organic compounds.

According to B. his reagent gives a slate grey colour turning to blue with the juices of certain fruits and vegetables whose antiscorbutic properties are well known (e.g. grapes, tomatoes, cabbage, &c.). Barley, turnips, &c., which are useless in scurvy, give no reaction. Cabbage juice which has been subjected to prolonged boiling loses its positive reaction.

Several interesting observations were made in the course of the experiments. The juice of a potato extracted in the presence of an acid gives a positive reaction, but if the acid is omitted or is added subsequently no reaction is obtained. The urine of a man whose diet contains a good proportion of antiscorbutic agents, gives a positive reaction.

B. tried his reagent with a variety of phenol compounds with negative results, except in the case of hydrokinone which gives a sharp blue reaction.

J. R. P.

Bedson, S. P. Blood platelet anti-serum, its specificity and rôle in the experimental production of purpura. *J. Path. & Bacteriol.*, 1921, **24**, 469.

In 1914 Ledingham showed that a serum prepared by inoculating the blood platelets of guinea-pigs into rabbits gave rise in guinea-pigs to a condition closely resembling purpura haemorrhagica in man. It was also shown that sera prepared against other blood elements had not this effect. When however the antiplatelet serum was tested *in vitro* it was found to agglutinate and lyse red blood corpuscles at a higher titre than that at which it agglutinated and altered platelets. The present author, following up this work, has prepared antisera to the various blood elements of the guinea-pig and has tested their agglutinative properties against the various antigens employed in their preparation. Antiplatelet, anti-red-cell, antileucocyte, antiserum, and anti-whole blood sera were prepared and tested for agglutinin and also in absorption experiments, the conclusion being reached that antiplatelet serum contains a specific body for platelets. An antileucocyte serum is unable to agglutinate platelets, and similarly an antiplatelet serum is devoid of action on leucocytes. When an antiplatelet serum is absorbed with red corpuscles any red cell agglutinins are removed while the platelet agglutinins remain. In absorption of a platelet serum with platelets there is a reduction of agglutinin both for platelets as well as red corpuscles. W. B.

Fåhræus, R. The suspension stability of the blood. *Acta med. Scandinavica*, 1921, **55**, 1–228.

This is an exhaustive monograph running to 228 pages and deals first of all with a careful historical review of the importance of the 'buffy coat' in the evolution of general pathological doctrines. The clinical significance of the buffy coat is next dealt with, as is also the development of its chemistry and physics. From his elaborate study of the older literature the author concludes that the *crusta sanguinis* or buffy coat is produced principally through agglutination of the red blood corpuscles giving rise to an increased sinking velocity of the latter. In other words, the buffy coat indicates a reduced suspension stability of the blood. The existence of the buffy coat was the basis of the humoral pathology from the time of Hippocrates to the middle of the nineteenth century. The substance of the buffy coat was considered to be the *materia morbi* and corresponded to the 'phlegm' of the older writers. It was on the existence of the buffy coat that the whole of the blood-letting therapy of the past was based. The author then describes his own observations on the suspension stability of the blood under different physiological and pathological conditions, especially pregnancy, and shows that the sinking velocity of the red corpuscles of human blood varies widely in different cases. Over 400 cases were examined, the results showing that the suspension stability is higher in the new born than in adults.

The author's method of experimentation was to draw blood from a vein and to add it to test-tubes containing 2 c.cm. of a 2 per cent. sodium citrate solution. The tubes were 17 cm. long and 9 mm. wide and had a mark indicating 10 c.cm. which was about 2 cm. from the mouth of the tube. The tube containing blood and citrate solution was turned up and down several times and the rate of sinking of the corpuscles determined.

In healthy men the average was 3·3 mm. per hour and in healthy non-pregnant females it was 7·4 mm.

During pregnancy the suspension stability is almost without exception greatly reduced (44·9 mm. per hour on an average). It was also reduced in almost all diseases examined. The author concludes that with a certain degree of probability all sinking values higher than 9 mm. per hour for men and 12 mm. per hour in non-pregnant women are to be regarded as pathological.

The increased sinking velocity of the red corpuscles, which by the stability reaction has been shown to exist during pregnancy and many diseases, is dependent on two factors. One is the increased agglutination of the corpuscles, and the other is their decreased number. Stokes's law regarding the motion of particles through a fluid medium is then applied by the author to get an approximate idea of the size of the corpuscle aggregates in different degrees of agglutination. This latter is chiefly dependent on the properties of the plasma. The agglutination here in question is identical with the rouleaux formation of the red corpuscles, and the increased agglutination is only an exaggeration of this normally existing phenomenon. Solutions of the different protein fractions of the plasma differ greatly in agglutinating capacity. Whilst serum albumin agglutinates the corpuscles only slightly, the globulins do so strongly. Fibrinogen is more active in this respect than serum globulin. The strong agglutinating effect of fibrinogen is also shown by the fact that it is greatly reduced by defibrination of the blood. That the agglutination capacity is really a property of the protein constituents of the blood is strongly supported by the fact that other emulsoids e.g. gelatin, also produce rouleaux formation. There are reasons to suppose that different degrees of agglutination capacity depend upon the colloidal state of these substances. A parallelism also exists between the agglutinating capacity of these proteins and their precipitation by neutral salts, the easiest precipitated being the most agglutinating. Furthermore, there seems to exist a connexion between agglutination and viscosity. Heating of serum or plasma at higher temperatures (48°–60° C.) increases their agglutinating capacity. This fact is against another possible explanation, viz., that the normal rouleaux formation or the exaggeration of this phenomenon should depend on the existence or the appearance of an agglutinin resembling those developed by specific immunization. During those conditions in which the agglutination is increased, either the serum globulin or the fibrinogen or both these substances, are increased in amount. It has also been shown that the plasma of the rapidly settling blood distinguishes itself by the fact that the first trace of protein precipitation is produced by addition of less neutral salt than that required for plasma of normal blood. All these plasma changes seem, to a certain degree, to be coincident and to be regarded as expressions for an alteration of the colloidal state of the plasma. For this the author uses the expression 'globulin increase'. The conclusion is made that the globulin increase is the most important cause of the increased rouleaux formation and of the increased sinking velocity of the red corpuscles, i.e., of the reduction in the suspension stability of the blood.

Incidentally a method is given by means of which the different protein constituents may be quantitatively determined in minute amounts of plasma. (Serum albumin, serum globulin, and fibrinogen.)

The reduced suspension stability of the blood, i.e. the increased agglutination of the red corpuscles can be demonstrated in the living organism in the following ways—

(*a*) In the blood flowing through the capillaries, directly.
(*b*) In the cutaneous veins.
(*c*) In the retinal vessels through breaking off the blood flow.

The reduced suspension stability of the blood is presumed to have a styptic effect and play an important part in the genesis of thrombi. It as much concerns the red parts of the mixed thrombi in the larger vessels, as the hyaline thrombi of the capillaries. The latter, according to the statements of literature are composed of fused red corpuscles and especially characterize the changes of the body organs in eclampsia. The suspension stability of the blood can be reduced through injection of gelatin solution and increased by injection of physiological, or better, hypertonic, NaCl solution.

The commonest and most important fact leading to the origin of fibrin-coagula in the dead body is the reduced suspension stability of the blood, i.e., the increased agglutination of the red corpuscles.

The suspension stability of blood is changed when it or one of its constituents is kept for some hours at different temperatures. The agglutinating power of serum and plasma is reduced by heat at temperatures between 30° and 48° C. This effect is strongest at about 42° C. and does not occur if the serum tests are shaken during the heating. Temperatures higher than 48° increase the agglutinating power of serum and plasma. The agglutinability of the red corpuscles is reduced at temperatures between 36° and 40° C., the maximum effect being produced at this latter temperature. At 48° and higher, haemolysis is produced. The reduction of the agglutinability of the corpuscles at the above mentioned temperatures is not prevented by shaking. If the defibrinated or citrated blood, in its entirety, is heated to different temperatures and shaken meanwhile, the agglutination of the red corpuscles is considerably reduced at temperatures above 42° C. W. A. M. S.

Zibordi, D. Su un particolare reperto nei leucociti eosinofili del cane. [**Peculiar finding in eosinophil leucocytes of dogs.**] *Haematologica*, 1920, **1**, 450–3.

In the bone-marrow, spleen and circulating blood of dogs infected with *Taenia cucumerina*, leucocytes were found provided with uncommonly large eosinophil granules. This finding has a certain importance as it might, if confirmed, support the view that eosinophil granules originate from ingested particles of fragmented red blood corpuscles. C. d. F.

Micheli, F. Sul significato clinico e biologico della proteinuria di Bence-Jones. [**On Bence-Jones's proteinuria, its clinical and biological significance.**] *Haematologica*, 1921, **2**, 1.

Investigations were carried out in a fatal case of lymphosarcoma of the large intestine in which a remarkable degree of Bence-Jones's proteinuria was observed. The interest of the case lay in the fact that no macroscopic or microscopic lesions of the bone-marrow could be detected. The Bence-Jones's albumose was found to be present in the urine, blood and effusions from serous cavities. According to the author it is not a regressive product of some albumin, but a true protein similar to that of the blood-serum. Special sets of experiments showed that it has a peculiar antigenic power due to two principal types of receptors. Of these one is present in small quantities and has properties identical to those of the proteins of the normal blood-serum; the other is present in a larger quantity and possesses properties so strictly specific that it might be safely termed the receptor or antigen of Bence-Jones's protein. C. d. F.

Bonnert, D. The prognostic value of Weiss's urochromogen reaction in pulmonary tuberculosis. *Tubercle*, 1921, **2**, 537–41.

Since January 1, 1917, Bonnert has compared Weiss's urochromogen or permanganate reaction with Ehrlich's diazo reaction in every case of pulmonary tuberculosis admitted to his hospital, and he repeated the test every month in every case. Of the 1,000 cases thus examined, 850 gave a negative reaction to both tests, and 108 gave a positive reaction to both. Of the 42 cases in which the reactions disagreed, 41 gave a positive urochromogen reaction, and only 1 a positive diazo reaction. In early amyloid disease the urochromogen reaction was positive in 91·7 per cent., while the diazo reaction was positive only in 55 per cent. Conclusion: the urochromogen test is cheaper, simpler and more delicate than the diazo test, and, as earlier publications show, a positive reaction to either test is usually of sinister omen. C. L.

Wahlberg, J. Bör diazoreaktionen i den kliniska diagnostiken ersättas med Weiss' urokromogenreaktion? [B.] [**Should the diazo reaction as a clinical test be replaced by Weiss's urochromogen reaction?**] *Finska Läk-sällsk. Handl.*, 1921, **63**, 360–7.

Wahlberg's comparison of the diazo with the urochromogen reaction is unfavourable to the former. In 294 cases of pulmonary tuberculosis, D. was positive in 45, or 15·3 per cent., and U. in 147, or 50 per cent. The frequency of the positive reactions increased with the severity of the disease, but the prognostic importance attaching to these reactions was somewhat diminished by the fact that in some cases discharged as much improved both reactions were positive, whereas others, which terminated fatally, consistently showed negative reactions. In 24 out of 40 cases of typhoid fever, and in 79 of 161 cases of paratyphoid fever the urochromogen reaction was positive. This was found to be much more delicate than the diazo reaction, as well as being cheaper and simpler. C. L.

Wöhlisch, E. Untersuchungen über Blutgerinnung (Beitrag zum Hämophilieproblem). [**Researches on blood coagulation (a contribution to the haemophilia problem).**] *München. med. Wchnschr.*, 1921, **68**, 1382.

In spite of many researches, even in modern times, the exact causation of the failure of haemophilic blood to clot must be regarded as unsettled. The prevailing view based upon the researches, especially of Sahli and of Morawitz and J. Lossen seems to be that the essential deficiency in the haemophilic blood is to be found in the thrombokinase. Sahli in particular stated that when haemophilic blood was mixed with the blood corpuscles of a haemophilic the delay in clotting was much greater (2½ hours) than when the same blood was mixed with corpuscles from a normal individual. The present author has made a number of tests on the blood of three individuals who, although there was no very good history of the disease in the family, seem to have been genuine haemophilics. He finds that the quantity of fibrin in the clotted haemophilic blood is normal; the osmotic resistance of the blood is normal and the coagulation quickening power of the haemophilic serum is normal. There is great delay in the coagulation of haemophilic blood. Contrary to Sahli he finds that this is not due to a defect in the blood corpuscles of the haemophilic blood, for control blood was mixed with suspensions of blood corpuscles of normal and haemophilic individuals and no essential difference in coagulation time was noticed. W. B.

Businco, A. Di un particolare meccanismo patogenetico di certi aneurismi valvolari. [**On the pathogenesis of certain valvular aneurysms.**] *Pathologica*, 1921, **13**, 61.

Description of two cases of aneurysm of the mitral valve from the study of which the author deduces that mitral aneurysms may have a mechanical and inflammatory origin. In the first case the pre-existence of an aortic valvular defect (insufficiency) is necessary, the mechanical factor being represented by a particular direction of the regurgitation current. An anomalous insertion or a shortening of the chordae tendineae as well as the oedema of the cusps may be different predisposing conditions favouring the action of the mechanical factor. In the second case the primary lesion is inflammatory and ulcerative in character, the ordinary blood-pressure acting as a secondary, though likewise necessary, factor,

C. d. F.

Giavotto, G. Contributo alla conoscenza dei carcino-sarcomi della tiroide. [**On mixed tumours of the thyroid.**] *Pathologica*, 1921, **13**, 95.

Description of a case of carcino-sarcoma of the thyroid. According to the author mixed new growths of the sort should be termed 'combination or collision tumours' as proposed respectively by Saltykow (*Centralbl. f. allg. Path. u. path. Anat.* 1905, **16**, 547) and by R. Meyer (*ibid.* 1919, **30**, 291). Both denominations are taken to mean that histogenetically different tumours may develop in the same organ, and contract relations varying according to their different biological activities. C. d. F.

Sotti, G. Contributo allo studio ed alla conoscenza dell' emangioma cavernoso della vescica urinaria. [**On cavernous haemangioma of the urinary bladder.**] *Pathologica*, 1921, **13**, 135, 164, 186.

Cavernous haemangioma can be considered as one of the relatively rare new growths of the urinary bladder. It consists chiefly of erectile tissue, viz., of many intercommunicating spaces or lacunae filled with blood and generally lined with an endothelium. The tumour is, as a rule, situated among the muscular layers, and surrounded by a connective tissue capsule containing a certain number of elastic fibres. The histological discrimination between cavernous haemangioma and simple vascular hyperplasia may often be very difficult or even impossible, so that many authors are of the opinion that no exact delimitation exists between the two pathological conditions. As to the histogenesis, Sotti thinks that the vascular lacunae forming the cavernous haemangioma, probably originate from a connective tissue 'embryogenetically and organogenetically angioplastic'.

C. d. F.

Bruzzone, C. Un caso di melanosarcoma della mucosa nasale. [**A case of melanotic sarcoma of the mucous membrane of the nose.**] *Pathologica*, 1921, **13**, 161.

Primary melanotic sarcomata of the nose are very rare. According to the author only 18 cases have been reported up to the present as being of this nature. Of these one has been recorded in this country by G. Wilkinson (*J. Laryngol.*, 1912, **27**, 1) who points out that some of the cases are rendered doubtful by the absence of any description of histological findings. The case now described by Bruzzone is the 19th of the series and was observed in a man of 55 years of age. The tumour was very malignant in character, and recurred in spite of three operations. C. d. F.

Cesaris-Demel, A. L'endiapedesi nel processo inflammatorio. [**Endiapedesis in inflammatory processes.**] *Haematologica*, 1920, **1**, 33.

During the formation of an inflammatory exudate, plasma and then blood corpuscles migrate through the unruptured wall of blood-vessels into the affected tissues. The phenomenon is generally termed *diapedesis* ; but according to the author it should be more appropriately spoken of as the '*ec-diapedesis*', this term indicating in a precise manner the outward passage of blood-plasma and blood corpuscles. On the other hand, when an inflammatory exudate is re-absorbed an inward passage of the same elements takes place, which the author proposes to indicate as the *endiapedesis.* This return of blood corpuscles, but chiefly of leucocytes, from the tissues into the blood-stream can be shown by means of *intra-vitam* staining methods of circulating blood corpuscles. In animals experimentally affected by an inflammatory process this method reveals the presence of leucocytes which, because of their morphological and tinctorial properties, can be considered with certainty as originating from the inflamed region. The changes shown by such leucocytes are degenerative and phagocytic in character, and correspond to the various phases of the inflammatory process. Thus the endiapedesis studied by means of *intra-vitam* staining methods becomes valuable as a new means for ascertaining the existence of deeply situated inflammatory foci and for following their evolution.

C. d. F.

Ferrata, A. Sulla patogenesi e sull' essenza dell' anemia a tipo pernicioso. [**On the pathogenesis and essence of pernicious anaemia.**] *Haematologica*, 1920, **1**, 48.

The author expresses himself on the subject as follows: (1) The presence in the blood and haemopoietic organs of primitive erythroblasts (megaloblasts) and primitive erythrocytes (megalocytes) points to a return to an erythrocytic type proper to the prehepatic haemopoietic period of embryonic life, when primitive erythroblasts are formed directly from haemo-histioblasts. (2) The 'megaloblastosis' and 'megalocytosis' cannot be considered as a consequence of severe myeloid changes due to a sort of vicarious function of the myeloid tissue. In fact many severe forms of anaemias are characterized by a normoblastic type of erythropoiesis, and megaloblasts and megalocytes make their appearance only when such anaemias assume a pernicious character. If the blood changes characteristic of pernicious anaemias were only the expression of a compensating erythropoiesis one would find, in the foci of extra-medullary haematopoiesis.

normoblastic elements similar to those characteristic of non-pernicious forms of experimental or spontaneous anaemias. One finds instead a great number of megaloblasts indicating that the same alteration affects the 'primordial haemo-histioblastic cell' in the bone-marrow, liver, and spleen. (3) Pernicious anaemia is, therefore, pathogenetically characterized by a 'haemo-histioblastic pre-haemocytoblastic or pre-myeloid orientation' viz., by a 'direct derivation of megaloblasts from clasmacytoid haemo-histioblasts.'

C. d. F.

Foà, P. Sul linfogranuloma. **[On lymphogranuloma.]** *Haematologica*, 1920, **1**, 17.

Description of three cases of particular interest because of the variety of the macro- and microscopic findings. The first one had all the characteristics of the usual type of lymphogranulomatosis. The bacteriological investigation of fragments of the affected lymph glands was attended by negative results. But the inoculation of the same material into guinea-pigs gave origin to a disease transmissible from animal to animal and characterized by the production of granulomata of lymph glands, spleen, and liver. Within these granulomata nodules were detected consisting chiefly of giant cells. In some specimens acid-fast bacilli were found. The second case had the macroscopic appearances of a common tuberculosis of the lymph glands, liver, and spleen. The histological picture was that considered by Sternberg as typical of lymphogranulomatosis. Bacteriological investigations were likewise attended by negative results. Inoculations into guinea-pigs were successful, but the picture was that of typical tuberculosis. The third case was macroscopically characterized by a haemorrhagic form affecting the lymph glands, liver, and spleen. Microscopic investigations revealed a diffuse lymphogranulomatosis. C. d. F.

BIOCHEMISTRY

Vitamin symposium. *J. Indust. & Engin. Chem.*, 1921, **13**, 1102.

In the above symposium, held in the Division of Biological Chemistry, American Chemical Society, in September 1921, contributions are given by R. A. Dutcher on factors influencing the vitamin content of foods; A. D. Emmett on standardized methods for the study of vitamins; R. R. Williams on vitamins from the standpoint of structural chemistry; V. K. La Mer on vitamins from the standpoint of physical chemistry; C. Funk on the anti-beri-beri vitamin; A. Seidell on experiments on the isolation of the anti-neuritic vitamin; A. F. Hess on the antiscorbutic vitamin.

These short papers are of interest to those concerned with accessory food factors, as they give the most recent results of work in this field, and a discussion of them from the American point of view. C. G. L. W.

Cowgill, G. R., and **Mendel, L. B.** **Studies in the physiology of vitamins. I. Vitamin B and the secretory function of glands.** *Am. J. Physiol.*, 1921, **58**, 131.

The water-soluble vitamin B does not stimulate pancreas, liver, and salivary gland to secretory activity. The intestinal mucosa of polyneuritic dogs contains secretin. These experiments, therefore, do not support the view that the function of vitamin B is to stimulate these glands.

W. C.

Steenboek, H., **Nelson, E. M.**, and **Hart, E. B.** **The incidence of an ophthalmic reaction in dogs fed on fat-soluble vitamin-deficient diet.** *Am. J. Physiol.*, 1921, **58**, 14.

Dogs, like other animals, develop an ophthalmia when the fat-soluble vitamin is withheld. This ophthalmia is cured by the administration of the vitamin in the form of cod-liver oil. The length of time in which this ophthalmia made its appearance in three dogs after withholding the vitamin was 67 days, 83 days, and 94 days respectively. The paper contains some other data concerning the effect on dogs of vitamin deficiencies.

W. C.

Holt, L. E., and **Fales, H. L.** **The food requirements of children. Protein requirements.** *Am. J. Dis. Child.*, 1921, **22**, 371.

A study of the diets taken by 100 healthy children of well-to-do parents. The amount of protein in the diets ranged from an average of 44 gm. per diem in the second year to 130 gm. in the fifteenth year. At one year the amount of protein per kgm. of body-weight averaged about 4 gm. daily, fell to 2·6 gm. at 6 years, and remained at this level till growth had ceased. Very active children consume exceptionally large amounts. Thus an active boy of 14 years of age took as much as 210 gm. daily. About two-thirds of the protein taken was of animal origin, and one-third vegetable.

O. L. V. de W.

Davidsohn, H. Neuere Arbeiten zur Physiologie und Pathologie der Magenverdauung beim Säugling. [**Physiology and pathology of gastric digestion in infants.**] *Arch. f. Kinderh.*, 1921, **69**, 142.

A review of recent work. O. L. V. de W.

Heyer, G. R. **Gastric secretion in man, with particular reference to psychic influence. I. Amount of juice and its digestive strength.** *Arch. f. Verdauungskr.*, 1921, **27**, 227. (*Chem. Abstr.*. 1921, **15**, 2479.)

Heyer put his patient to sleep by suggestion, then removed the stomach contents, tested its acidity, and by hypnotic suggestion or 'psychic' feeding of blood, milk, or bouillon, produced an increase in gastric secretion accompanied by an increase in proteolytic activity. These psychically induced alterations lasted for only a few minutes, and not for hours as Pavlov reported in his studies; but they are none the less striking.

C. G. L. W.

Lanz, W. The theory and technique of the determination of the acidity of gastric contents. *Arch. f. Verdauungskr.*, 1921, **27**, 282. (*Chem. Abstr.*, 1921, **15**, 2649.)

This is probably the most critical discussion of the problem of the determination and significance of gastric acidity that has appeared for some time. The general conclusions are that the actual acidity is best determined by the gas-chain method; however, for secretion poor in protein, good results are given by the indicator series, methyl violet, dimethylaminoazobenzene, methyl red, p. nitrophenol, rosolic acid, or neutral red naphtholphthalein. Titration with phloroglucin-vanillin gives only approximate results. The 'true' acidity, i.e. the true base-combining power of the juice, cannot be measured. Instead, the 'total acidity' or the 'neutralizing power' is measured and is not much different in protein poor juice from the 'true' acidity. This determination is made by titration with 0·1 N. NaOH and phenolphthalein as an indicator. The potential acidity cannot be directly measured, but is obtained by subtracting the 'actual' acidity from the 'total' acidity. C. G. L. W.

Staub, H. Formation of enzymes. *Helvetica Chim. Acta*, 1921, **4**, 281. (*Chem. Abstr.*, 1921, **15**, 2888.)

The ability of the body to assimilate 20 gm. of glucose, taken by the mouth, may be measured by the duration and degree of the resulting hyperglycaemia. The ability is good if carbohydrates have been given within a reasonable time, and is decreased after deprivation of carbohydrate. On a diet containing carbohydrate, the assimilation enzymes which govern intermediary carbohydrate metabolism are present in the organism in sufficient quantities to present an excessively high alimentary glycaemia, and to facilitate rapid assimilation. After deprivation of carbohydrates, a scarcity of these enzymes exists, and therefore an imperfect power of assimilation. Hence, in the normal metabolism of carbohydrates, it is a question of the secretion of enzymes to meet conditions. After ingestion of carbohydrates, enzymes are secreted in excess for the assimilation of food and are present in the body ten to fifteen hours later in so abundant an amount that ingested glucose is promptly assimilated. On deprivation of carbohydrates for a longer period than this, a shortage of carbohydrate-assimilating enzymes gradually occurs, since no demand for them exists. If glucose is then ingested, at first it is assimilated with difficulty, or not at all, and the alimentary hyperglycaemia attains a high value. However, the ingested glucose then acts as a stimulus for the secretion of enzymes; and, as soon as this secretion has begun—it occurs quickly—a decrease in the percentage of blood-sugar and a return of the latter to its normal level takes place. A specific formation of these enzymes occurs in man if carbohydrates be ingested in physiological amounts. These enzymes may be designated equilibrium enzymes, since they restore the equilibrium which has been destroyed by too high a concentration of an ingested substance in the blood. C. G. L. W.

MacNider, de B. W. Relation between the amount of stainable lipoid material in the renal epithelium and the susceptibility of the kidney to the toxic effect of the general anaesthetics. *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 289.

As functional tests for the kidney, phthalein excretion, diuretics, and determinations of the R P_H, creatinin and urea of the blood were employed.

Histologically the deposition of stainable lipoid material in the renal epithelium was studied. Some relationship appears to exist between the stainable lipoid and susceptibility to an anaesthetic. The amount of lipoid material, as determined histologically, increased after an anaesthetic, and the increase is apparently associated with functional damage. Anaesthetics are more toxic for the kidneys of old animals than young. Chloroform is more toxic than ether, and the renal epithelium of naturally nephropathic dogs is more susceptible than that of normal dogs.
O. L. V. de W.

Magath, T. B. A test for early renal insufficiency. Preliminary paper. *J. Lab. & Clin. Med.*, 1921, **6**, 463. (*Chem. Abstr.*, 1921, **15**, 2492.)

Caffeine citrate caused a rise in the uric acid value of the blood in nephritics, piling up in the blood either uric acid or a substance giving a blue colour with the Folin and Wu reagent for uric acid. In general, the test checked closely with the clinical findings. C. G. L. W.

Squier, T. L., and **Newburgh, L. H. Renal irritation in man from high protein diet.** *Arch. Int. Med.*, 1921, **28**, 1. (*Chem. Abstr.*, 1921, **15**, 2905.)

Four patients with hypertension, but without definite evidence of renal involvement, were given a high protein diet (100–200 gm.) for periods of two to three weeks. After such feeding, the urines of all contained albumin and red blood cells, although both had previously been absent. After a return to a low protein diet, both albumin and blood cells disappeared from the urine. In three of these patients the enlargement and oedema of the retina were increased by the high protein diet. A similar experiment was performed on a patient with low blood-pressure, but with an active nephritis as judged from clinical findings and the presence of albumin in the urine. The high protein diet was followed by an increased albuminuria and the appearance of red blood cells. Two men, in whom the existence of a nephritis was discovered in the course of this work, ate large amounts of meat at two meals on one day. Albumin, which was absent before the experiment, promptly appeared in the urine of both and red cells in one. A similar experiment upon five normal young men was followed by the appearance of red blood cells in the urine of all. C. G. L. W.

Brunn, F. Beiträge zum Diabetes insipidus. [**Diabetes insipidus.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 176.

Three cases of polyuria, of which two are considered by the author to be true diabetes insipidus, are described. Experiments were made by giving the patients water with and without the addition of salt, and with pituitrin. The amount of urine passed at short intervals was noted, and the concentration of albumin and salt in the blood-serum determined. Thirsting experiments were also performed.

In the two cases of true diabetes insipidus the results of the influence on the concentration of albumin in the serum were only qualitatively different from what occurs in normal subjects when water or abstention therefrom occurred. When, however, salt was added to the water there was a cardinal difference from normal behaviour. The diabetics eliminated water as if salt were not present. The blood behaved as normal. Hence, in diabetes insipidus neither hydraemia nor sodium chloride concentration of the serum have a pronounced effect on elimination. In these cases the active kidney is more independent of these factors than the normal organ.

C. G. L. W.

Benedict, S. R., and Osterberg, E. A method for the determination of sugar in normal urine. *J. Biol. Chem.*, 1921, **48**, 51.

A new method of estimating sugar is described. Both creatinine and sugar under the right conditions give a colour with picric acid in alkaline solution. By the addition of a suitable amount of acetone the colour due to the creatinine may be destroyed without injury to the colour due to the sugar. By the use of the method therefore the determination of sugar in the presence of a large amount of creatinine becomes possible. When applied to the urine direct the method gives rather high results. The difficulty can be eliminated by the treatment of the urine with specially treated commercial bone charcoal. The authors have thoroughly tested the method. In the course of the paper they claim that the ordinary view that the compound of creatinine and picrate in alkaline solution is picramic acid, is incorrect. The compound, though it has the same formula as picramic acid, has very different physical properties and stability. R. A. P.

Shaffer, P. A. Antiketogenesis I and II. *J. Biol. Chem.*, 1921, **47**, 343.

The author has found that *in vitro* aceto-acetic acid is oxidized in alkaline solution, if glucose is also present. In the absence of glucose it is not oxidized. Fructose or glycerol will exert a similar action, but not lactic acid. He thinks that this *in vitro* analogy is suggestive in connexion with the known effect of carbohydrate in reducing the amount of ketone bodies present in the organism. Working upon this analogy as a basis, he has gone over the literature dealing with ketosis in some detail and come to the conclusion that it is possible to distinguish between ketogenic and antiketogenic bodies in the organism. If this is done a balance can be struck between the amount of either being metabolized in a given experiment. In illustration: fat and glucose can be regarded respectively as keto- and antiketogenic in character. When the balance is struck at the point at which the ketone bodies appear in the urine, it is found that the ratio of ketogenic to antiketogenic factors is a molecular one. Some ground is therefore given for thinking that in the organism the riddle as to the function of carbohydrate in reducing ketosis may have a definite chemical basis. R. A. P.

Utheim, K. Metabolism studies in infants suffering from chronic nutritional disturbances (Athrepsia). *Am. J. Dis. Child.*, 1921, **22**, 329.

A study of the chronic condition of extreme malnutrition in children occurring independently of known infection, and unaccompanied by acute gastro-intestinal or nervous symptoms. Confirms the finding of Freund that the athreptic infant shows a diminished power of oxydizing benzol (administered by the mouth) to phenol. The benzol was apparently absorbed, as judged by analysis of the stools. In athreptic infants the caloric nitrogen ratio and the carbon/nitrogen ratio of the urine are raised. This rise was not accounted for by an increase in the creatinine, uric acid, or amino acid content of the urine, but an increased organic acid content, with corresponding rise in ammonia, was present. These organic acids, insoluble in ether, are to be regarded as products of disturbed metabolism. A greatly increased proportion of the total food ingested was lost in the stools of the athreptic as compared with the healthy infant. O. L. V. de W.

Bailey, C. V. Apparatus used in the estimation of basal metabolism. *J. Lab. & Clin. Med.*, 1921, **6**, 657.

The author gives in detail a description of a semiportable apparatus consisting of a gasometer combined with a modification of the French gas mask and English valves which can be used for determining basal metabolism. For analysis of the respiratory products a modification of Haldane's apparatus is employed. Full instructions are given in the technique of handling the apparatus and of conducting a test. The apparatus is used principally in the diagnosis and prognosis of thyroid disease. The result of the test frequently determines when serious operative procedures can be undertaken with least risk to the patient. C. G. L. W.

Stewart, G. N. Possible relations of the weight of the lungs and other organs to body-weight and surface area (in dogs). *Am. J. Physiol.*, 1921, **58**, 45.

Observations on 12 dogs varying from 36·7 kgm. to 2·7 kgm. The weight of certain internal organs varies with the surface, that of other organs varies with the weight of the animal. The weight of liver, stomach, intestine, kidneys, and lungs varies with the surface, the weights of spleen and heart with the body-weight. In all cases the organs were blood free when weighed.

It is pointed out that the weight of the blood-free lungs is roughly proportional to their vascular capacity, since the thin pulmonary membrane is largely covered with capillaries. W. C.

Stewart, G. N. The pulmonary circulation-time, the quantity of blood in the lungs, and the output of the heart. *Am. J. Physiol.*, 1921, **58**, 20.

The paper contains a critical discussion of the methods used to determine the pulmonary circulation-time in dogs and actual estimations in a number of dogs of different sizes. From this factor and the minute volume of the heart the quantity of blood in the lungs can be calculated. The results are given in tabular form and do not lend themselves to a summary.

Direct estimations of the amount of blood contained in the lungs under different conditions were also made in a few dogs.

Condition of Animal.	Quantity of Blood in Lungs.	Total Blood in Lungs and Heart.
Bled to death	3 %	
Killed instantaneously by electric current	9 %	25 %
Outflow from right heart blocked	3·5 % to 9 %	
Outflow from left heart blocked	22 %	27 % to 30 %

W. C.

Briggs, A. P., and **Shaffer, P. A.** **The excretion of acetone from the lungs.** *J. Biol. Chem.*, 1921, **48**, 413.

These experiments show in a striking way that the amount of acetone excreted from the lung in ketosis bears an absolute relation to the amount of acetone in the blood. The coefficient of distribution of acetone for water and air was found to be 334 for water/air at 37° C. and 750 mm. Under the same conditions the coefficient for blood-serum and air was found to be 337. The ratio of acetone in blood to that in the alveolar air was 333. The agreement is sufficiently close to establish the point that acetone is excreted from the lungs by a physical process of diffusion. This was also found to apply in the case of the kidneys.

It follows from this that a determination of the amount of acetone in the breath affords a reliable indirect method of estimating the amount of acetone in the blood. It also follows that, if the excretion of urine during a given period is not excessive, the amount of acetone excreted by means of the breath in a given time may greatly exceed the amount excreted by the kidneys. R. A. P.

Van Slyke, D. D. **Studies of acidosis. XVII. The normal and abnormal variations in the acid-base balance in the blood.** *J. Biol. Chem.*, 1921, **48**, 153.

This paper does not lend itself to abstraction. It should be read by those interested in the subject. Van Slyke points out that there are nine theoretical possible relations between the reaction of the blood and the concentration of the blood bicarbonate. These are made up as follows: The blood bicarbonate may be high, low, or normal. In each of these conditions the reaction of the blood may be high, low, or normal. There is only one normal condition for the bicarbonate and the reaction of the blood. In the earliest papers published by the author, reference was only made to two conditions, viz. that in which the bicarbonate was low and the reaction normal, and that in which the bicarbonate was very low and the reaction of the blood more acid than the normal. In the last few years other possible conditions have been realized, experimentally at least. Some of them have been found clinically.

The author summarizes under the various headings the evidence for the occurrence of the various types of abnormalities with quotations from the literature. R. A. P.

Ringer, M., and **Underhill, F. P. (Nos. VII, VIII, and IX)**; **Underhill, F. P.**, and **Long, M. L. (No. X)**; **Underhill, F. P.**, **Greenberg, P.**, and **Alu, A. F. (No. XI)**. **Studies on the physiological action of some protein derivatives. VII. The influence of various protein split products on the metabolism of fasting dogs. VIII. The influence of nucleic acids on the metabolism of fasting dogs. IX. Alkali reserve and experimental shock. X. The influence of nucleic acids on the metabolism of the fasting rabbit. XI. The influence of some protein split products upon the metabolism of fasting rabbits.** *J. Biol. Chem.*, 1921, **48**, 503.

The so-called peptone shock, due to the injection of peptone-like substances into the blood, has called forth a large literature, related as it is to the problems of anaphylactic shock and also of shock in wound infection. The suggestion has been made by Whipple and Cook that every inflammatory process is fundamentally a proteose intoxication. They found that the production of inflammatory processes called forth an increased urinary N excretion. Their work followed upon the discovery that the injection of proteose reproduced in dogs the intoxication of intestinal obstruction.

In the above series of papers, increased excretion of urinary N, creatin, and phosphate is taken as an index of tissue catabolism. It is shown that the catabolic effect produced in dogs by the injection of proteoses intravenously is a specific effect of the proteose type of compound. It is produced by impure and pure proteoses, by proteins with the exception of gelatin. Amino-acids and histamine are without the effect. Interestingly enough, yeast nucleic acid produces the effect, whereas animal nucleic acid does not. The fall in the alkaline reserve produced is ascribed to the decreased excretion of urine consequent upon the fall of blood-pressure.

Rabbits do not react to the injection of peptone in as violent a way as the dog, yet show the catabolic effect of the injection of yeast nucleic acid and of proteoses. For this reason it is considered that the effect is not essentially due to the toxic nature of the injected material, but is in some way dependent upon the 'detrimental action incident to the introduction of a foreign protein into the circulation'. R. A. P.

Barach, L. A., and **Woodwell, M. N.** **Studies in oxygen therapy, with determinations of the blood gases.** *Arch. Int. Med.*, 1921, **28**, 367.

The oxygen saturation of both venous and arterial blood was studied. In all the cardiac cases an arterial (anoxic) anoxaemia was present, attributable to associated pulmonary conditions. Cardiac dyspnoea seemed to have little relation to the degree of anoxaemia, either anoxic or stagnant. Oxygen inhalation relieved the anoxaemia in all cases, but gave little relief to the dyspnoea. The dyspnoea in cardiac cases is probably associated with an impaired elimination of carbon dioxide, with resulting diminution in the alkali reserve of the blood, or an actual lowering of its P_H. In nearly all cases the oxygen venous saturation was increased by oxygen inhalation. On pneumonia and broncho-pneumonia prolonged administration of oxygen (30 minutes to two hours) appeared to give satisfactory clinical results. The inhalation almost invariably increased the arterial oxygen saturation or raised it to a normal figure. In pneumonia the difference between arterial and venous saturation was generally normal or even less than normal, indicating an increased blood-flow. Cyanosis in this disease is associated with an increased oxygen capacity of the blood, due to increase in the haemoglobin percentage, which appears with improvement. A true stagnant anoxaemia may be observed in pneumonia.

In two cases of lethargic encephalitis the development of an extreme type of shallow breathing was attended by deep cyanosis and coma. An arterial anoxaemia was present with excess of carbon dioxide in the arterial blood. The inhalation of oxygen relieved the anoxaemia, but a steady increase in carbon dioxide occurred, leading in one case to an uncompensated carbon dioxide acidosis.

Gas analyses were made by the Van Slyke-Stadie method. An apparatus for administering oxygen is described. O. L. V. de W.

Nash, T. P., and Benedict, S. R. The ammonia content of the blood and its bearing upon the mechanism of acid neutralization in the animal organism. [**B.**] *J. Biol. Chem.*, 1921, **48**, 463.

This paper opens up an interesting new field. The question of the amount of ammonia in the blood has been for some time a debatable one for various reasons, the estimation alone involving considerable difficulty. The low values for the ammonia of the normal circulating blood found by Folin and Denis and Barnett have been confirmed by the use of an improved method of estimation. Normal values are of the order of 0·1 mgm. of ammonia nitrogen per 100 c.cm. of blood. As the amount of ammonia in the circulating blood is so low, how can the large amounts of ammonia excreted in normal urine be accounted for? 'A calculation will make clear the nature of the problem. If the rate of blood-flow through the kidneys is 150 c.cm. per minute per 100 gm. of kidney tissue, and the total weight of kidney tissue is 300 gm., then the 24-hour volume of blood passing through the kidneys is 648 litres. Assuming that 100 c.cm. of arterial blood contains 0·1 mgm. of ammonia, and that this is completely removed, the total output of ammonia nitrogen in the urine in 24 hours would be 0·648 gm. This value is very close to that actually found for the normal average individual, but the assumed figure for arterial blood is higher than that which we usually found, and it is scarcely conceivable that the kidney is 100 per cent. efficient in the excretion of ammonia.' They go on to point out that the ammonia content of blood is at any rate inadequate to account for the high urinary ammonia in certain pathological cases. The problem therefore is limited to three possibilities, either (*a*) the blood ammonia is higher than that apparently found, or (*b*) ammonia is present in some easily dissociable complex in the blood, or (*c*) the kidney itself forms the ammonia which it eliminates. The experimental part deals with these three possibilities.

It is shown that blood contains very little ammonia and that standing for 20 minutes leads to the splitting off of a slightly greater quantity than the analysis done upon the fresh sample. A further standing of the blood sample, however, leads to the appearance of no more ammonia. This disposes to a large extent of possibilities (*a*) and (*b*). It is further found that under the conditions of the experiments hens' albumin does not decompose to form ammonia. Further ammonia added to blood can be recovered by analytical methods completely.

The next step was to determine whether the incubation of blood with acids (such as lactic acid) led to the appearance of any ammonia which could be considered as having been used in neutralization of the acid added. No extra ammonia appeared. It was further found that in one case of phloridzinized dogs, excreting larger quantities of ammonia than the normal, there was no increase in the amount of ammonia in the blood. Finally the experiments of Winterberg, and of Henriques and Christiansen upon the amount of ammonia in the blood of animals after ligature of the ureters or double nephrectomy, were repeated upon dogs. It was fully confirmed that under these conditions there was no increased ammonia in the blood. In fact in these cases the lowest recorded values for ammonia in the blood were obtained.

The above experiments seemed to point to the fact that the kidneys themselves formed ammonia which they excreted. Confirmation of this view was found in the fact that the blood of the renal vein was found to contain about twice as much ammonia as blood from other sources, such as the carotid artery or vena cava.

In a discussion of the bearing of the new facts upon current views of acidosis, it is pointed out that depletion of the alkali reserve may occur under three definite conditions. First, acid radicles may be introduced into the blood too rapidly for elimination by the kidney, or for the powers of the kidney to make ammonia for neutralization. Secondly, the kidney may lose its power of excreting acid radicles, its power of ammonia production being normal. Thirdly, the kidney may lose its power of making ammonia. In all these cases there will be neutralization of acids with fixed bases or with proteins, and so depletion of the alkali reserve. The view taken is that the first condition occurs in diabetes, and the last two in nephritis. On this view, depletion of the alkali reserve is primarily a kidney disease.

It is thought that urea is the probable precursor of the ammonia formed by the kidney. R. A. P.

Inchley, O. A simple method for the determination of the coagulation-time of blood in animals. The influence of the electric current on the absorption of drugs. *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 237, 241.

A simple method of determining the coagulation-time of blood is described in which a drop of blood is placed on a vertically rotating wire and the moment at which the drop ceases to slide along the wire is determined. With this apparatus the author ascertained that a 1 per cent. solution of calcium chloride driven in through the skin by a current of 20 milliamperes distributed over an electrode surface of 40 sq. cm. diminished the clotting-time of the blood from 100 seconds to 45 seconds. Experiments were made with atropine, aconitine, adrenalin, and strychnine; all these substances were driven in by the electric current.

Iron, calcium, cyanides, salicylates, ferricyanides, also reach the general system when cataphoretically applied. C. G. L. W.

Kramer, B., and Tisdall, F. F. The direct quantitative determination of sodium, potassium calcium, and magnesium in small amounts of blood. *J. Biol. Chem.*, 1921, **48**, 223.

A method is described for the determination of the elements mentioned in 7 c.cm. samples of blood.

Proteins are removed by the use of trichloracetic acid. The results are in fair agreement with the results obtained by ashing blood samples. The concentrations found for the elements in 100 c.cm. of human blood were for sodium 170–225 mgm.; potassium 153–201 mgm.; calcium 5·3–6·8 mgm.; magnesium 2·3–4·0 mgm. R. A. P.

Boström, E. F. Conditions causing an unequal distribution of erythrocytes in the blood-stream. *Am. J. Physiol.*, 1921, **58**, 195.

Under certain conditions. after asphyxia, abdominal pressure, adrenalin, there is a sudden increase in the number of red cells per unit volume. This has been held to be a real increase and has been attributed variously to increase in the plasma volume or to formation of new cells, or to bringing into the circulation cells stored away in some internal organ.

It is shown in this paper that the increase is not general but is accompanied by a decrease in the number of cells in the heart-blood. An accumulation of red cells in the peripheral tissues was found to be associated with the two following factors: (1) lowering of surface temperature; (2) diminished oxygen supply to the tissues. The explanation is as follows: In blood with its normal alkalinity the blood cells and the endothelial cells carry negative charges. Since bodies with equal charges repel each other, this prevents the cells from adhering to one another and to the walls of the vessel. A small increase in the hydrogen-ion concentration of the medium would neutralize the negative charges of the cells and would therefore diminish a force that tends to keep them apart and away from the vessel wall. There would then be an accumulation of cells in the smaller vessels, preventing a condition similar to the one observed in stasis, where aggregations of cells can be seen to adhere to the vessel wall while the plasma is in motion.

It is shown experimentally that a local increase in the number of red cells can be produced by the injection of acid sodium phosphate. It is also shown that a suspension of red corpuscles in a solution of sodium carbonate and CO_2, corresponding in hydrogen-ion concentration to plasma, is stable when kept at 38° C. When the temperature is allowed to fall, the suspension becomes unstable and the corpuscles sink. It is known that the hydrogen-ion concentration of such a solution rises as the temperature falls.

The condition of asphyxia, adrenalin, and abdominal pressure produce vasoconstriction of the skin, leading to diminished oxygen supply with the formation of acid metabolites and lowering of temperature of the skin. The resulting increase in the hydrogen-ion concentration explains the increase in the number of red cells in the blood-vessels of the skin. It is briefly pointed out that such a factor may account for the capillary stasis in shock.

W. C.

Theis, R. C., and **Benedict, S. R.** **Distribution of uric acid in the blood.** *J. Lab. & Clin. Med.*, 1921, **6**, 680.

Through Benedict's investigations we know that uric acid circulates in the blood in two conditions, viz. free uric acid and that combined with other substances the combination of which is unknown. In the latter condition the acid does not respond to the ordinary qualitative and quantitative tests. With Miss Theis he has now determined the distribution of uric acid between the corpuscles and serum. In 50 per cent. of a series of cases uric acid was equally distributed between corpuscles and serum. In the remaining half of the cases the uric acid was higher in the serum. In a few cases it was lower in the serum. Pathological conditions did not influence the results.

There was a marked difference in the permeability of the corpuscles of certain bloods to added uric acid. This suggests that other cells of the body may show similar differences in permeability. These findings may tend to throw light on the questions involved in specific uric acid retention in the organism.

C. G. L. W.

Fitz, R., and **Bock, A. V.** **Studies on blood-sugar. The total amount of circulating sugar in the blood in diabetes mellitus and other conditions.** *J. Biol. Chem.*, 1921, **48**, 313.

By use of the vital red method of determining the volume of blood in the body, estimations of the total amount of sugar circulating in the blood have been made. In the case of 7 normal persons, this was found not to exceed 7·5 gm. The plasma sugar did not exceed 4·85 gm. It was found that there were considerable variations, a value as low as 1·64 gm. being recorded for the plasma sugar in one case. There was more sugar in the plasma than in the corpuscle. Diabetic bloods showed higher total sugar contents, as high as 10·8 gm. in one case for the plasma sugar. The main increase took place in the amount of sugar in the plasma. The conclusion is drawn that sugar in the diabetic is not carried mainly in the plasma. It is held that the amount of sugar in the urine bears relation not to the absolute percentage in the blood but to the total amount of sugar circulating. When the total plasma sugar rises above a value of 5·2–5·3 gm. there is excretion of sugar in the urine. It is hoped that it will be possible to work out a formula to express the relationship between the amount of sugar circulating in the blood and the amount excreted in the urine.

R. A. P.

Williams, J. L. Total non-protein nitrogenous constituents of the blood in chronic nephritis with hypertension. *Arch. Int. Med.*, 1921, **28**, 426.

No relationship was found between the height of the blood-pressure and the concentration of the non-protein nitrogenous constituents of the blood in 88 patients examined. High values for creatinine usually indicated a bad prognosis. In patients with both nephritis and myocardial inefficiency, the uric acid content of the blood was higher than in those with nephritis alone. Creatinine, uric acid, urea, and total non-protein nitrogen were studied. The average survival corresponded to the chemical findings.

O. L. V. de W.

Brugsch, T., Dresel, K., u. Lewy, F. H. Zur Stoffwechselneurologie der Medulla oblongata. II. Experimenteller Beitrag zur Regulation des Zuckerstoffwechsels in der Oblongata. [**An experimental study of sugar regulation as influenced by the medulla oblongata.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 262.

In a paper read by the author at the German Congress for Internal Medicine in 1920 it was shown that the piqûre point in the fourth ventricle was identical with the sympathetic vagus nucleus. They gave it the name ‘vegetative oblongata nucleus’. In stimulating it was found that hyperglycaemia did not always result. They have gone over the serial sections which were made of the place of injury and now find that when the posterior half, or rather the posterior third, was touched a hyperglycaemia resulted. In further experiments it is now shown that when the anterior half is stimulated a hypoglycaemia is produced. The anterior part of the nucleus is concerned with setting the adrenals in action, while the posterior portion controls the vagus fibres to the pancreas. C. G. L. W.

Mertz, A., und Rominger, E. Experimentelle Blutzuckeruntersuchungen bei Kindern. [**Blood-sugar researches in children.**] *Arch. f. Kinderh.*, 1921, **69**, 81.

In infants who have not been fed for four hours the average value of the blood-sugar is 0·081 per cent. The blood-sugar curve after oral administration of glucose reached its maximum in thirty minutes to one hour, and had fallen to a fasting value in three hours. The administration of 0·5 gm. tannic acid reduced the height of the hyperglycaemia produced by glucose, apparently owing to interference with absorption. Five children with icterus showed either a prolonged or increased alimentary hyperglycaemia. In two of these cases laevulose also produced a rise in the blood-sugar, but to a less extent than glucose. O. L. V. de W.

Moraczewski, V., et **Lindner, E.** Effets des injections intraveineuses sucrées. [**Effect of intravenous sugar injections.**] *J. de physiol. et de path. gén.*, 1921, **19**, 202.

Injections of dextrose and laevulose, besides producing glycosuria, increase the lactic acid of the urine and diminish the phosphoric acid excretion. Laevulose produces a febrile reaction and a leucopenia.

O. L. V. de W.

Welch, L. H., and **Hughson, W.** **Systemic effects of the intravenous injection of solutions of various concentrations, with special reference to the cerebrospinal fluid. The cerebrospinal fluid in relation to the bony encasement of the central nervous system as a rigid container. Intracranial venous pressure and cerebrospinal fluid pressure as affected by the injection of solutions of various concentrations.** [**B.**] *Am. J. Physiol.*, 1921, **58**, 53, 85, 101.

These three papers are so closely reasoned and contain such a large number of experimental data that they do not lend themselves readily to being abstracted. Of the main conclusions the following may be mentioned.

The results of the experiments confirm the older view of Monroe, Kellie, and Abercromby, that the cranium and vertebral canal form a rigid and closed mechanism. The ordinary physical laws of a 'closed box' may therefore be applied to the cranium, and conversely the integrity of the cranium is essential for the operation of these laws. The cranial cavity is fixed in volume and is completely filled by brain, cerebrospinal fluid, and blood. Variations in any one of the three may occur, compensation being afforded by alterations in the volume of one or both of the remaining two. The volume of the brain is not absolutely fixed, but within narrow limits physiological variations in its bulk can be produced.

The pressure of the cerebrospinal fluid is largely independent of cerebral arterial and cerebral venous pressure, but is modified by both. The intracranial arterial pressure is an important factor in maintaining the intracranial pressure conditions, but its importance may be over-emphasized. Minor slow alterations of the cerebral arterial supply have no effect on the pressure of either the cerebrospinal fluid or superior sagittal sinus. Marked sudden alterations, however, do affect their pressure. This influence of the arterial supply is of less physiological importance than is the venous pressure. The pressure of the cerebrospinal fluid in the etherized animal is always higher than that of the superior sagittal sinus. There is a marked correspondence between venous pressures as determined in the superficial brachial vein and in the superior sagittal sinus. W. C.

Schönfeld, H. Der Kreatingehalt des Froschmuskels im Zustande der hypnotischen Starre. [**The creatine content of frog muscle in hypnotic rigidity.**] *Arch. f. d. ges. Physiol.*, 1921, **191**, 211.

After several hours of rigidity the muscles showed an average increase of creatine of 21·4 per cent. C. L. E.

Hammett, F. S. (1). **Creatinine and creatine in muscle extracts. I. A comparison of the picric acid and the tungstic acid methods of deproteinization. II. The influence of the reaction of the medium on the creatinine-creatine balance in incubated extracts of muscle of the albino rat.** *J. Biol. Chem.*, 1921, **48**, 127.

Hammett, F. S. (2). **Studies of the thyroid apparatus. IV. The influence of parathyroid and thyroid tissue on the creatinine-creatine balance in incubated extracts of muscle tissue of the albino rat.** *J. Biol. Chem.*, 1921, **48**, 143.

These papers are representative of the modern tendency to apply boldly *in vitro* experience with extracts of tissues to the solution of the biochemical problems of the living organism.

It is found that extracts of the albino rat muscle tissue, when incubated with a physiological salt solution at an acid, neutral and alkaline reaction, show an increase in creatinine content in 24 hours, under sterile conditions. This creatinine must be coming from the creatine present originally because there is no change in the total creatinine obtainable from the muscle.

It is argued from this that a similar change, viz., conversion of creatine to creatinine, must occur in the tissue, especially because the maximum amount of the change takes place in the neutral mixture, i. e., at the reaction of the body. The increased creatine excretion observed in alkalosis and in acidosis is attributed to the fact that in acid and alkaline solution the rate of conversion from creatine to creatinine is slower.

The addition of a parathyroid extract to incubating mixtures of the type described leads to a decrease in the amount of creatinine formed from the creatine originally present, this decrease occurring in both acid, neutral, and alkaline mixtures, but to the greatest extent in the neutral mixtures. The effect is not obtained with thyroid extracts. The result seems to have some bearing upon the interrelation of the parathyroids and of the creatinine-creatine story with muscle tone, though the exact application of the work is not yet clear. R. A. P.

Meyerhof, O. Die Energieumwandlungen im Muskel. V. Milchsäurebildung und mechanische Arbeit. [**The energy exchanges in muscle. V. Lactic acid production and mechanical work.**] *Arch. f. d. ges. Physiol.*, 1921, **191**, 128.

The lactic acid fatigue maximum for frog's gastrocnemius stimulated in hydrogen or in Ringer's solution with single induction shocks is usually about 0·35 per cent.; but 0·5 per cent. can be obtained if the Ringer's solution is made alkaline (P_H ·10) with Na_2CO_3, and under these conditions the total anaerobic work done is increased, although the tension (in Kg.) per cm. of muscle per mg. lactic acid (the isometric lactic coefficient, or Km.) usually falls off somewhat. In such alkaline solutions about 20 per cent. of the lactic acid passes out into the solution, as against 5 per cent. under neutral conditions. Administration of $NaCO_3$ *per os* has no effect, nor has immersion of the muscle in slightly acid Ringer solution. The fatigue maximum, in other words, is conditioned by the lactic acid content of the muscle itself. The value of Km. falls as anaerobic fatigue progresses, if maximal shocks are employed, but not if the stimuli are submaximal; it is much reduced by alcohol, urethane, or chloral, and to a smaller extent by potassium salts. It is suggested that the narcotics remove the lactic acid from the contraction site. The author uses an inertia lever similar in principle to that used by Hill, and also an angular lever in which the load progressively diminishes to zero as contraction proceeds. The work deduced from tension-length diagrams is smaller than that deduced from Hill's formula. The work coefficient (Ka) of lactic acid is obtained from the work done and lactic acid produced, and would be expected to be about 8·2 (Kg.-cms. per mg.) = 47 per cent. anaerobic efficiency, but is actually much less, especially at higher temperatures or if the muscle is fatigued. The oxidative efficiency is half the anaerobic and is from 20–24 per cent. This agrees with work by others on the efficiency of the heart and of the whole body, where the most favourable conditions are present, yet efficiency does not exceed 30 per cent. (= 60 per cent. anaerobic). It is unlikely that the maximal potential energy set free in a muscle on stimulation ever exceeds 75 per cent. of the whole energy change. Some experiments on guinea-pig muscles gave results which were on the whole comparable with those obtained on frog muscle. C. L. E.

RADIOLOGY

Radiodiagnosis.

Kloiber, H. Die Röntgenuntersuchung der Darminvagination. [B.] [**Röntgen examinations in cases of intussusception.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 351.

An article of comparison has been contributed by Kloiber on the two methods of diagnosing intussusception under Röntgen control, a matter of great difficulty where, too often, the complaint will scarcely admit of much loss of time, but requires almost immediate operation.

He divides his paper into two parts: First, Röntgen examination by contrast means (*a*) after a barium meal, (*b*) after barium injection. Secondly, Röntgen examination without contrast means. Entering into various details as to the respective working of a barium meal and barium injection, he draws the conclusion that a barium meal, which to children should be given in milk, is more satisfactory in the results it gives for determining the character of the intestinal affection, because there is no danger of it being obstructed in its course through the intestine, and does not cause so much discomfort, whereas barium injection, although the quicker method, has a tendency to become obstructed through a constriction of the lumen, such as is observable in a tumour causing stenosis, thus rendering the Röntgen test ineffective. The writer, however, suggests, if there is time, that both the liquid meal and the barium emulsion for injection should be used.

Where haste is important he recommends Röntgen examination without contrast means, as not only does it in these acute cases save time, but avoids further discomfort and suffering to the patient, such as is caused by filling the intestine with a contrast meal or injection.

The writer gives an account of various cases both in infants and adults, and refers to considerable literature on the subject. F. E. R.

KURTZAHN, H. Veränderungen der männlichen Harnröhre im Röntgenbild nach Kontrastfüllung. [B.] [**Röntgen illustrations of changes in the male urethra after contrast injections.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 294.

Kurtzahn gives his experiences of the old methods of examining patients suffering from cystitis, prostatic hypertrophy, stricture with fistula, and injuries to the urethra. The results of observations under the old methods of filling the urinary bladder with 400 c.cm. of a 10 per cent. emulsion of bismuth, as practised by von Wulff and Albers-Schonberg, were not satisfactory, inasmuch as these injections often left a bismuth deposit in the bladder, especially in the diverticula, later often leading to the formation of concretions. Even stronger solutions of 10 per cent. bismuth subnitrate showed no good photographic results, and the introduction of insufflation was abandoned when it was found that embolism sometimes resulted, and one fatal case was quoted by Lewien.

The new method for diagnosis has proved highly satisfactory although there is necessity for the greatest caution in its use. The results have been still better since Praetorius has substituted colloidal silver iodide, 'pyelon' for collargol.

In the new method described by Kurtzahn a solution of pure barium sulphate was used in proportion of 1 in 3. The solution previous to use was sterilized by boiling and strained. Collargol did not commend itself to him, and the cost of colloidal silver iodide made it impracticable, and 10 per cent. solution of calcium iodide did not give a sufficiently intense shadow.

The method of procedure used was to place the patient on his side at an angle of 45°. A sterilized Nelaton catheter was introduced into the urethra to a depth of about 3 cm. The urethra was compressed with two fingers. During the use of the rays the injections were continued in order that all pockets and niches of the urethra might be filled and so bring them under radiographic observation.

Kurtzahn concluded his observations by stating that no bad effects resulted from this method, and his diagrams show that not only cases of stricture, urethral fistula, &c., were clearly represented for diagnosis, but it was even possible to localize early stricture of the urethra, more particularly in the prostatic parts. F. E. R.

Radiotherapy

BÉCLÈRE et **SIREDEY.** Un cas de pseudo-hermaphroditisme androgyne avec tumeur intra-abdominale consécutive à l'ablation d'un rudiment de glande génitale. Disparition rapide de cette tumeur sous l'influence de la radiothérapie. [**A case of androgynous pseudo-hermaphroditism with an intra-abdominal tumour following the removal of a rudimentary genital gland. The rapid disappearance of this tumour under radiotherapy.**] *J. de radiol. et d'électrol.*, 1921, **5**, 211.

The authors describe the clinical features of a case of a woman of 54, who had an abdominal tumour which appeared to be a large bossy tumour of the spleen. Some points about the case resembled that of a porter seen nine years previously by Béclère, in which the tumour followed on the removal of a neoplasm of the left testicle. Two important facts were observed in the present case: (1) A cystic tumour had been removed from the left inguinal region four years previously. (2) The patient had never menstruated. From a clinical examination it appeared that the case was one of androgynous pseudo-hermaphroditism; the external genital organs and the breasts were female in type, and a small mass under the skin at the upper part of the right labium magus immediately below the external inguinal ring was looked upon as a rudimentary testicle. The cystic tumour previously removed from the left side had not been microscoped, but a description by the surgeon strengthened the belief that the mass on the right side was a rudimentary testicle. The inguinal tumour and the large splenic tumour were regarded as cause and effect, and, since operation was refused, radiotherapy was the only available treatment; treatment lasted about five months and comprised twenty séances, weekly at first and then at longer intervals. A description is given of the method of applying the rays. The results obtained were very good and rapid; ten days after the first séance the tumour was distinctly smaller and the pain caused by it considerably less. Six weeks from the beginning of treatment, radioscopic examination of the abdomen showed nothing abnormal; a month later the patient had no pain and the spleen was palpated with difficulty. Irradiation was continued as a precaution against recurrence. Later the patient put on weight, but she complained that brain-work was more difficult and tiring than formerly.

The latter part of the paper is taken up by an account of the case treated some years previously by Béclère. P. L.-B.

Parrisius, W. Warnung vor Überdosierung bei Bestrahlung von Fällen von myeloischer Leukämie. [**Warning against overdosage in the radiotherapy of myeloid leukaemia.**] *Strahlentherapie*, 1921, **12**, 234.

The author here publishes a series of five cases of myeloid leukaemia as a warning and in the hope that others may thereby be enabled to avoid certain unpleasant results of too vigorous treatment. He disagrees with the view expressed by Klewitz that in the X-ray therapy of these cases 'the spleen should receive a daily radiation of half an erythema dose, under control of the blood picture—the radiation to be continued until the blood picture is nearly normal.'

Full details are given in each case of the dosage of X-rays adopted and of the series of blood counts made. The cases which were treated with half erythema doses all showed a rapid loss of strength after radiation, with symptoms of heart-failure, rapid destruction of leucocytes, and shrinkage of the spleen. Three of these ended fatally, either during or shortly after the course of treatment.

The author concludes that no general rule can profitably be laid down as to the dosage in myeloid leukaemia, and that it is wise to begin treatment with quite small doses and to note how the patient responds before proceeding. In this way an exact idea can be obtained of the degree of sensitiveness to the rays displayed by the individual patient. The best guides are the well-being of the patient, the haemoglobin content of the blood, the leucocyte count, and the general blood picture. Technical improvements in modern apparatus have not resulted in corresponding improvements in the result of treatment. Quite as good results were formerly obtained with old types of apparatus. Hence it appears that small amounts of radiation are sufficient to produce changes in an organism suffering from a myeloid condition.

E. M. W.

Bacmeister, A. Die Röntgenbehandlung der Lungen- und Darmtuberkulose. [**X-ray treatment of pulmonary and intestinal tuberculosis.**] *Strahlentherapie*, 1921, **12**, 225.

The use of X-rays in the campaign against tuberculosis is year by year becoming of greater importance. The good results of radiation in tuberculosis of glands, soft parts, bones, joints, epididymis, and the uterine adnexa are now well established. But while radiotherapy has been making rapid strides in this direction, it has progressed but slowly in the field of pulmonary tuberculosis and is still regarded with some distrust. This on the whole is fortunate, since great harm may be done by careless or mistaken use of the rays. A firm foundation for the radiotherapy of pulmonary tuberculosis was first laid by the work of Küpferle and Bacmeister, who showed that proliferating tuberculous granulations could be converted into scar tissue while the tubercle bacilli present showed no definite evidence of damage. The law, that hard X-rays exert a selective action upon tuberculous granulation tissue, holds in every case of tuberculosis, including, of course, pulmonary disease. The treatment of pulmonary cases is a much more difficult and delicate matter than that of any other form of tuberculosis. X-Rays can convert either a slowly progressive or a rapidly growing granuloma into scar tissue, but are useless where the virulence of the infection overcomes the resistance of the organism and the bacilli are not held in check, as in cases of cavity formation and caseation, and in all rapidly progressive lesions or those where there is acute destruction of tissue. Radiotherapy merely stimulates or reinforces a pre-existing reaction of the tissues towards repair, and its great therapeutic value lies in the fact that definite cicatrization may be initiated by it. If results are to be obtained and accidents avoided, a proper selection of cases must be made. This, however, is only possible after correct evaluation of the pathological-anatomical findings. Only slowly progressive, stationary, or latent types of scirrhosis or nodular forms of the disease should be treated by X-rays. Furthermore, deep therapy of the lung should never be undertaken except after long clinical study of the patient and after a good radiograph has been obtained. The treatment is aimed at the production of a definite febrile reaction. A proper technique is of fundamental importance. Too much stress cannot be laid upon the fact that only by the closest attention to technique, by the greatest care in working, and an accurate selection of cases, can results be achieved. Each case must receive individual consideration and each be given its appropriate dosage and technique. With the technique at present in use ambulatory radiotherapy of pulmonary tuberculosis is absolutely to be rejected. During the period of treatment an irritation of the irradiated areas frequently occurs, manifesting itself by increased sputum, cough, general nervousness, and prostration. Subsequently there follows a certain quite characteristic discomfort due to cicatrization—slight dragging pain and a sensation of pressure in the irradiated areas—while the symptoms of pulmonary disease disappear.

Multiple large ports of entry are used, with small doses and long intervals. The author goes fully into the questions of technique and dosage, the latter varying from case to case. He discusses this and gives directions for modifying the treatment in accordance with the symptoms that arise.

Latterly, unusually good results have been obtained in the treatment of intestinal tuberculosis by X-rays. The patients dealt with were not the hopelessly progressive pulmonary cases with a terminal infection of the bowel, but cases of stationary chronic phthisis, with a relatively good general condition, but in whom an intestinal infection had developed and occupied the foreground of the clinical picture.

When the site of infection cannot be accurately determined, large ports of entry are used over the ileo-caecal region and the course of the large intestine. In not a few cases the symptoms—fever, diarrhoea, pain—have rapidly disappeared. The results are as a whole very good and the author warmly recommends this method of treatment. E. M. W.

Radiobiology.

Leitch, A. The immediate effects of X-rays on the blood lymphocytes. *Arch. Radiol. & Electroth.*, 1921, **26**, 122.

Leitch criticizes the evidence brought forward recently by Russ and his collaborators to show that a short exposure to X-rays (a few seconds to ten minutes) produces an average reduction of 50 per cent. in the number of lymphocytes circulating in the blood of the rat. The essence of his criticism lies in his insistence upon the great variations found under normal conditions in this animal, and in his suggestion that the effects noted are due to manipulation and fright, and not to the irradiation. The importance of the question is seen in respect of a possible similar effect in man and the influence such lymphopenia—if it exist—may exert upon the course of tumour growth when treatment by radiotherapy is being carried out. Though two rats subjected to X-rays for five minutes showed the result noted by Russ, similar investigations carried out on man proved inconclusive; indeed, the only case in which there was a noteworthy drop in number of circulating lymphocytes was a highly nervous woman. Comparisons were therefore made of 'docile' and 'nervous' rats, and though the number of experiments appears to have been too small for dogmatism, dummy experiments in which X-rays were cut out and other variations made convince the author that any fall in lymphocytes under small doses of irradiation must not be ascribed to the irradiation, but are susceptible of one or other of the explanations given above. Leitch expressly notes that he cannot say what may be the effects of large or repeated exposures. The conditions in Leitch's and in Russ's sets of experiments were not identical, and how far this may account for the difference in conclusions arrived at by these workers it is impossible to say.

W. S. L.-B.

Russ, S. The immediate effects of X-rays on the blood lymphocytes. *Arch. Radiol. & Electroth.*, 1921, **26**, 146.

This paper constitutes the reply of Russ on behalf of himself and his colleagues to the criticism of their results by Leitch (see above). Russ agrees that Leitch's X-ray exposures were probably closely similar to those employed in the researches under criticism, but maintains that the effects noted were true X-ray effects on two grounds. The first is the parallelism between the duration of X-ray exposure and the time necessary for re-establishment of the normal blood condition. Thus

Exposure for 1 hour results in death of animal.

Exposure for 30 minutes leads to a lymphocyte reduction of about 50 per cent., and time for recovery is about 2 to 3 weeks.

Exposure 5 minutes, lymphocyte reduction about 50 per cent., time for recovery about 1 to 2 weeks.

Exposure 1 minute, lymphocyte reduction about 50 per cent., time for recovery about 1 to 3 days.

Exposure 12 seconds, lymphocyte reduction about 50 per cent., time for recovery about 1 day.

Exposure 2 seconds, lymphocyte reduction about 40 per cent., time for recovery about 1 day or less.

Exposure $\frac{1}{5}$ second, lymphocyte reduction about 20 per cent., time for recovery about 1 day or less.

The second ground for his belief that the effects noted were due to X-rays and not to shock or other accidental causes lies in experiments carried out to investigate this very point. In two sets (each of 10 animals) the rats were handled similarly and the X-ray apparatus was run similarly, but the one set of animals was adequately shielded by lead from the rays, while the other set received irradiation over a period of two minutes. Blood counts were taken before and one hour after the test. The percentage lymphocyte changes were as follows:

Control rats: + 69, + 64, + 32, + 16, + 13, + 10, + 8, 0, – 13, – 40.

Irradiated rats: – 62, – 58, – 57, – 56, – 55, – 54, – 54, – 43, – 34, – 33.

Under exposure to radium for a time ensuring the same surface exposure as a 12 seconds exposure to X-rays similar lymphocytic reductions were observed; here the element of disturbance is reduced to a minimum. Russ, in his turn, criticizes Leitch's evidence in support of the latter's opinion that the change is due to fright, and submits that, in view of the very large amount of experimental evidence from several laboratories that the circulating lymphocyte (not only of the rat but of many of the smaller animals) is a very vulnerable type of cell to X-rays, the evidence adduced by Leitch is insufficient. W. S. L.-B.

Tiebig, H. Durch Reizbestrahlung der Leber beschleunigte Blutgerinnung. [**Effect of stimulative irradiation of the liver on blood-coagulation.**] *Zentralbl. f. Chir.*, 1920, **47**, 1389. (*Fortschr. a. d. Geb. d. Röntgenstrahlen.*, 1921, **28**, 93.)

Examination of the statements of Stephan and Jurasz concerning acceleration of blood coagulation by means of irradiating the spleen furnished substantially the same results. The normal time of coagulation determined by the Fornio method was 10–14 minutes. Irradiation of the spleen (Intensiv-Reform-apparatus, Fürstenau-Coolidge-tubes, focus distance from skin 33 cm., 2 mm. aluminium filter, diameter of field 6–8 cm., period of irradiation 8 minutes, i.e. about half an erythema dose) gave a mean acceleration of coagulation, 43·4 per cent. of the normal. Stimulative irradiation of the liver increases formation and excretion of fatty acids and enzymes, and accelerates, as in the case of irradiation of the spleen, the coagulation-rate of the blood. By combined stimulation of the liver and spleen the mean period before coagulation set in was reduced to 51·6 per cent. of the normal. An altered coagulation-rate was still recognizable in almost all cases on the third day after irradiation. S. U. L.-B.

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